Section 1

Disease From Potential Bioterrorist Agents

Anthrax

Woolsorters' Disease, Cumberland Disease, Maladi Charbon, Malignant Pustule, Malignant Carbuncle, Milzbrand, Splenic Fever

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Anthrax results from infection by *Bacillus anthracis*, a spore forming, Gram positive aerobic rod (family Bacillaceae).

Geographic Distribution

Anthrax can be found worldwide; it is particularly common in parts of Africa, Asia and the Middle East. In the United States, foci of infection occur in South Dakota, Nebraska, Mississippi, Arkansas, Texas, Louisiana and California, with smaller areas in other states.

Transmission

In animals, transmission is usually by ingestion. Herbivores usually become infected when they ingest spores on plants in pastures. Outbreaks typically occur in neutral or alkaline calcareous soil and are often associated with heavy rainfall, flood or drought; under optimal levels of moisture, temperature and other conditions, spores in the soil can revert to the vegetative form and grow to infectious levels. Contaminated bone meal and other feed can also spread this disease. Carnivores usually become infected after eating contaminated meat. Vultures and flies may spread anthrax after feeding on carcasses.

In infected animals, large numbers of bacteria are present in the hemorrhagic exudates from the mouth, nose and anus; when they are exposed to oxygen, these bacteria develop endospores and contaminate the soil. Sporulation requires oxygen and does not occur inside a closed carcass; opening an infected carcass for necropsy should be avoided. Anthrax spores can remain viable for decades in the soil or animal products such as dried or processed hides and wool. Spores can also survive for 2 years in water, 10 years in milk and up to 71 years on silk threads. Vegetative organisms are thought to be destroyed within a few days during the decomposition of unopened carcasses.

Humans usually develop the cutaneous form of anthrax after skin contact with infected animal tissues such as hides, wool, bone meal and blood. Biting flies that feed on infected animals or carcasses may also be able to transmit this form. Inhalation anthrax is seen after inhalation of spores from contaminated dust or animal products. Intestinal anthrax results from the ingestion of contaminated meat containing viable spores.

Anthrax has been studied as a weapon by the United States, Iraq, the former Soviet Union and probably other countries.

Disinfection

Anthrax spores are resistant to heat, sunlight, drying and many disinfectants. Spores can be killed with 2% glutaraldehyde formaldehyde or 5% formalin; soaking overnight is recommended. A 10 % NaOH or 5 % formaldehyde solution can be used for stockyards, pens and other equipment. Sterilization is also possible by heating to 121°C for at least 30 min. Blowtorches can be used to disinfect buildings.

Exposed arms and hands can be washed with soap and hot water then immersed for one minute in a disinfectant such as an organic iodine solution or 1 p.p.m. solution of mercuric perchloride. Clothing should be cleaned and boiled.

Infections in Humans

Incubation Period

The incubation period in humans is 1 to 7 days; typically, symptoms of inhalation anthrax appear after 2 to 5 days and symptoms of cutaneous anthrax after 2 to 3 days. After accidental aerosol release in the Soviet Union, cases continued to appear for up to 6 weeks.

Clinical Signs

Three forms of disease are seen in humans: cutaneous anthrax, intestinal anthrax and inhalation anthrax.

Cutaneous anthrax is characterized by a papular skin lesion, which becomes surrounded by a ring of fluid–filled vesicles. The central papule ulcerates, dries and develops a depressed, black scab. The skin lesion is usually painless, but is often surrounded by significant edema. Swelling on the face or neck may occlude the airways; lesions on the face or neck can also develop into meningitis. Fever, lymphadenopathy, pus and pain are seen only if secondary infections occur. Lesions often resolve spontaneously but disseminated, fatal infections occur in approximately 20%.

Intestinal anthrax develops after eating contaminated meat. The initial symptoms may be mild and can include malaise, a low fever and mild gastrointestinal symptoms. Severe symptoms then develop acutely and may include high fever, dyspnea, cyanosis, disorientation and other signs of septicemia. Intestinal anthrax rapidly progresses to shock, coma and death.

Inhalation anthrax occurs after inhaling spores in contaminated dust. Natural infections are mainly seen among workers who handle infected hides, wool and furs. The clinical signs develop gradually and are nonspecific. Symptoms may include fever, tiredness, and malaise; a nonproductive cough and mild chest pain may be present. The symptoms often improve for several hours to 3 days; this period of improvement ends with the acute onset of severe respiratory distress, diaphoresis, stridor and cyanosis, followed by fatal septicemia and shock within one to two days.

Communicability

Person to person transmission of anthrax is very rare and has been reported only in cases of cutaneous anthrax.

Diagnostic Tests

Anthrax is diagnosed by finding the characteristic organisms in clinical samples or by isolating *B. anthracis*. Blood, fluid samples from skin lesions, aspirates of lymph nodes or spleen, or cerebrospinal fluid (in cases of meningitis) are stained with polychrome methylene blue (M'Fadyean's stain). *B. anthracis* organisms are square–ended, blue–black bacilli surrounded by a pink capsule. Bacteria are not always found in blood cultures during septicemia.

B. anthracis colonies on blood agar are white or gray, at least 3 mm diameter, nonhemolytic, and have a dry, ground–glass appearance and sometimes tails. Capsules may be demonstrated in mucoid colonies from cultures grown on nutrient agar with 0.7 percent sodium bicarbonate, incubated overnight under CO_2. *B. anthracis* is also susceptible to specific bacteriophages and exhibits a characteristic 'string–of–pearls' formation when grown with penicillin. Antibiotic treatment of patients may prevent isolation of the organism.

Treatment and Vaccination

Natural strains of *B. anthracis* are usually susceptible to a variety of antibiotics; most but not all natural strains are susceptible to penicillin. Effective treatment depends on early recognition of the symptoms: treatment for cutaneous anthrax is usually effective but inhalation and intestinal forms are difficult to recognize and mortality rates are much higher. Inhalation and intestinal anthrax may be fatal once symptoms appear, in spite of treatment. Supportive therapy may be necessary. Vaccines are available for humans who have a high risk of infection.

Morbidity and Mortality

In most countries, cases of anthrax occur infrequently and sporadically, mainly as an occupational hazard among veterinarians, agricultural workers, and workers who process hides, hair, wool and bone products. The cutaneous form accounts for more than 95% of natural anthrax infections. The intestinal form is rare but can occur in outbreaks associated with contaminated meat. Natural cases of inhalation anthrax are rare; however, aerosolized biological weapons would be expected to produce a high percentage of this form.

Estimates of the case fatality rates of untreated cutaneous anthrax range from 5 to 25%, while treated cutaneous anthrax has a very low mortality rate. Untreated inhalation and intestinal infections are almost always fatal; these infections may also be recognized too late for effective treatment. The case fatality rate for the intestinal form is estimated to be from 25% to 75%; the case–fatality rate for inhalational anthrax probably approaches 90 to 100%.

Infections in Animals

Species Affected

Many species can develop anthrax but susceptibility varies: rats and chickens are relatively resistant to disease while goats, sheep, cattle and horses are more susceptible. Anthrax has been seen in pigs, mink, cats and dogs fed contaminated meat.

Incubation Period

The incubation period is 1 to 20 days; most infections become apparent after 3 to 7 days. In pigs, the incubation period is usually 1 to 2 weeks.

Clinical Signs

In ruminants, sudden death may be the only sign. Staggering, trembling and dyspnea may be seen in some animals, followed by rapid collapse, terminal convulsions and death. In the acute form, clinical signs are apparent for up to 2 days before death. Fever and excitement may be followed by depression, stupor, disorientation, muscle tremors, dyspnea, abortion, congested mucous membranes and bloody discharges from the nose, mouth and

anus. Chronic infections, characterized by subcutaneous edematous swellings, are also seen; the ventral neck, thorax and shoulders are most often involved. This swelling may be widespread.

In horses, common symptoms include fever, chills, anorexia, depression and severe colic with bloody diarrhea. Swellings may be seen in the neck, sternum, lower abdomen and external genitalia. Affected animals usually die within 1 to 3 days but some animals can survive up to a week.

Sudden death may also be seen in pigs. Many pigs have mild chronic infections characterized by localized swelling, fever and enlarged lymph nodes, with eventual recovery. Some animals develop progressive swelling of the throat, with dyspnea and difficulty swallowing; these animals may suffocate. Intestinal involvement, with anorexia, vomiting, diarrhea or constipation, is less common. Recovered, asymptomatic animals may have signs of localized infections in the tonsils and cervical lymph nodes at slaughter.

Clinically apparent anthrax in dogs, cats and wild carnivores resembles the disease in pigs.

Communicability

Yes. Large numbers of bacteria are present in the carcass and in bloody discharges from body openings. Tissues including skin and wool can contain spores, which remain viable for long periods of time.

Diagnostic Tests

A presumptive diagnosis is often made by examining blood or other tissues for the characteristic bacteria. Blood clots poorly in anthrax cases and sampling may be done post–mortem. In pigs, bacteremia is rare and a small piece of aseptically collected lymphatic tissue is often used. *Bacillus anthracis* is a large Gram positive rod that may occur singly, in pairs or in chains; endospores are not formed inside the body but may be found under certain culture conditions.

Bacterial culture may be used for diagnosis. *B. anthracis* colonies on blood agar are white or gray, at least 3 mm diameter, nonhemolytic, and have a dry, ground–glass appearance and sometimes tails. Capsules may be demonstrated in mucoid colonies from cultures grown on nutrient agar with 0.7 percent sodium bicarbonate, incubated overnight under CO_2. *B. anthracis* is also susceptible to specific bacteriophages and exhibits a characteristic ‘string–of–pearls’ formation when grown with penicillin.

Other diagnostic methods include polymerase chain reaction to detect bacterial nucleic acids, immunofluorescence for bacteria in blood or tissues, or a chromatographic assay to detect antigens in the blood. Mouse or guinea pig inoculation is rarely used. Immunoblotting (Western blotting) and enzyme–linked immunosorbent assays (ELISAs) are available; however, serology is rarely used for diagnosis.

Treatment and Vaccination

Antibiotics may be effective if treatment is started early. Vaccines are available for livestock.

Morbidity and Mortality

Clinical infections in ruminants and horses are usually fatal; pigs often recover. In carnivores, mortality is relatively low.

Post–Mortem Lesions

Rigor mortis is usually absent or incomplete and the carcass is typically bloated and decomposes rapidly. Dark, tarry blood may ooze from the body orifices. Edema may be noted, particularly around the throat and neck, in horses. Necropsies should generally be avoided, to prevent contamination of the surrounding area with spores.

If the carcass is opened, signs of septicemia will be evident. The blood is dark, thick and does not clot readily. Edematous, blood–tinged effusions may be seen in the subcutaneous tissues, between skeletal muscles and under the serosa of organs. Hemorrhages, petechia and ecchymoses are often noted in the lymph nodes, abdomen and thorax; hemorrhages and ulcers are also common in the intestinal mucosa. Peritonitis and excessive peritoneal fluid may be seen. The spleen is usually enlarged and has a ‘blackberry jam’ consistency. The lymph nodes, liver and kidneys may be swollen and congested.

Pigs with chronic anthrax usually have lesions only in the pharyngeal area. The tonsils and cervical lymph nodes are typically enlarged and a mottled salmon to brick–red color on cut surface. The tonsils may be covered by diphtheritic membranes or ulcers. The surrounding area is usually edematous and gelatinous. Some pigs may have a chronic intestinal form, with inflammation and lesions in the mesenteric lymph nodes.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/anthrax_t.htm

FAO Manual on meat inspection for developing countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

Material Safety Data Sheets–
Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology
http://www.gsbs.utmb.edu/microbook

The Merck Manual
http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook
http://www.vnh.org/BIOCASU/toc.html

References

"Anthrax." *Animal Health Australia.* The National Animal Health Information System (NAHIS), Oct 2001. 19 Nov 2002 <http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha>.

"Anthrax" *Centers for Disease Control and Prevention (CDC)*, December 2001. 19 Nov 2002 <http://www.cdc.gov/ncidod/dbmd/diseaseinfo/anthrax_t.htm>.

"Anthrax" In *Manual of Standards for Diagnostic Tests and Vaccines.* Paris: Office International des Epizooties, 2000, pp. 233–244.

"Anthrax." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 19 Nov 2002 <http://www.vnh.org/BIOCASU/6.html>.

"Anthrax." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 432–5.

Herenda, D., P.G. Chambers, A. Ettriqui, P. Seneviratna, and T.J.P. da Silva. "*Manual on meat inspection for developing countries*. FAO Animal Production and Health Paper 119." *Publishing and Multimedia Service, Information Division, FAO*, 1994. 19 Nov 2002 <http://www.fao.org/docrep/003/t0756e/T0756E03.htm#ch3.3.8>.

"Material Safety Data Sheet –*Bacillus anthracis*." *Canadian Laboratory Centre for Disease Control,* January 2001. 19 November 2002 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds12e.html>.

Turnbull, P.C.B. "*Bacillus*." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 19 November 2002 <http://www.gsbs.utmb.edu/microbook/ch015.htm>.

Turnbull, P.C.B. In *Zoonoses*. Edited by S.R. Palmer, E.J.L. Soulsby and D.I.H Simpson. New York: Oxford University Press, 1998, pp. 3–16.

Botulism

Lamziekte, Shaker Foal Syndrome, Loin Disease, Limberneck, Western Duck Sickness, Bulbar Paralysis

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Botulism is caused by botulinum toxin, a potent neurotoxin produced by *Clostridium botulinum* and a few strains of *C. baratii* and *C. butyricum*. *Clostridium botulinum* is an anaerobic, Gram–positive, spore–forming rod.

Botulism can result from the ingestion of preformed toxin or the growth of C. botulinum in anaerobic tissues. Seven types of botulinum toxin, designated A through G, have been identified. Types A, B, E and F cause illness in humans. Type C is the most common cause of botulism in animals. Type D is sometimes seen in cattle and dogs, and type B can occur in horses. Types A and E are found occasionally in mink and birds. Type G rarely causes disease, although a few cases have been seen in humans. All types of botulinum toxin produce the same disease; however, the toxin type is important if antiserum is used for treatment.

Geographic Distribution

C. botulinum is found worldwide and cases of botulism can be seen anywhere. In ruminants, botulism mainly occurs in areas where phosphorus or protein deficiencies are found. Botulism is seen regularly in cattle in South Africa and sheep in Australia. This disease is rare in ruminants in the United States, although a few cases have been reported in Texas and Montana.

Transmission

C. botulinum and its spores are widely distributed in soils, sediments in fresh and coastal waters, the intestinal tracts of fish and mammals, and the gills and viscera of shellfish. The bacteria can only grow under anaerobic conditions. Botulism occurs when animals ingest preformed toxins in food or C. botulinum spores germinate in anaerobic tissues and produce toxins as they grow.

Botulism in Humans

In humans, botulism is classified into three forms: foodborne, wound, and infant or intestinal botulism. Foodborne botulism is the most common form and occurs when humans ingest toxins in various foods. The foods associated with botulism are usually low acid (pH greater than 4.6) and may include home–canned foods, sausages, meat products, canned vegetables and seafood products. Commercial foods are occasionally implicated. Wound botulism occurs when an anaerobic wound is contaminated with C. botulinum, usually from the soil. Infant botulism is seen only in children less than a year of age. In this form, C. botulinum spores germinate in the intestinal tract and produce toxin. Honey has been associated with some cases of infant botulism but spores can also be found in many other sources. Adults with altered intestinal flora, secondary to gastrointestinal surgery or antibiotic therapy, may also be able to develop this form.

Botulism in Animals

Preformed toxins in a variety of sources, including decaying vegetable matter (grass, hay, grain, spoiled silage) and carcasses can cause botulism in animals. Carnivores, including mink and commercially raised foxes, usually ingest the toxins in contaminated meat such as chopped raw meat or fish. Cattle in phosphorus–deficient areas may chew bones and scraps of attached meat; a gram of dried flesh may have enough botulinum toxin to kill a cow. Similar cases occur in Australia, where protein–deficient sheep sometimes eat the carcasses of rabbits and other small animals. Ruminants may also be fed hay or silage contaminated by toxin–containing carcasses of birds or mammals. Horses usually ingest the toxin in contaminated forage. Birds can ingest the toxins in maggots that have fed on contaminated carcasses or in dead invertebrates from water with decaying vegetation. Cannibalism and contaminated feed can also result in cases in poultry.

The toxicoinfectious form of botulism corresponds to the wound and intestinal forms in humans. C. botulinum may grow in necrotic areas in the liver and GI tract, abscesses in the navel and lungs, or anaerobic wounds in the skin and muscles. This form of botulism appears to be responsible for shaker foal syndrome in horses. Toxi-

coinfectious botulism is also seen in chickens, when broilers are intensively reared on litter; the cause of this phenomenon is unknown.

Botulinum and Bioterrorism

In a bioterrorist attack, botulinum toxin could be delivered by aerosols, as well as food or water. After aerosol transmission, the clinical disease is expected to be similar to foodborne botulism.

Disinfection/ Inactivation

Botulinum toxins are large, easily denatured proteins. Toxins exposed to sunlight are inactivated within 1 to 3 hours. Botulinum can also be inactivated by 0.1% sodium hypochlorite, 0.1N NaOH, heating to 80°C for 30 minutes or 100°C for 10 minutes. Chlorine and other disinfectants can destroy the toxins in water.

The vegetative cells of *Clostridium botulinum* are susceptible to many disinfectants, including 1% sodium hypochlorite and 70% ethanol. The spores are resistant to environmental conditions but can be destroyed by moist heat (120°C for at least 15 min).

Infections in Humans

Incubation Period

The incubation period for foodborne infections is a few hours to 10 days; most cases become symptomatic after 18 to 36 hours. Wound infections may become evident within a few days to 2 weeks. The incubation period for intestinal or infant botulism is unknown. Inhalation botulism usually develops 12 to 36 hours after exposure, but in some cases the incubation period may be up to several days.

Clinical Signs

Foodborne Infections

In foodborne infections, gastrointestinal disturbances – including nausea, vomiting and abdominal pain – are often the first sign. Either diarrhea or constipation may occur. As the disease progresses, a symmetric, descending flaccid paralysis develops in the motor and autonomic nerves. The clinical signs may include blurred or double vision, photophobia, drooping eyelids, slurred speech, dysphagia, urine retention, a dry mouth and muscle weakness. In untreated progressive infections, descending paralysis of the respiratory muscles, arms and legs is seen. Fatal respiratory paralysis may occur within 24 hours in severe cases. Fever is not usually seen.

Wound Botulism

Wound botulism is very similar to foodborne infections; however, gastrointestinal signs are not usually present and patients may have a wound exudate or develop a fever.

Infant Botulism

Most cases of infant botulism occur in 2–week to 6–month–old babies. The first symptom is usually constipation. Other signs may include lethargy, weakness, excessively long sleep periods, diminished suck and gag reflexes and dysphagia with drooling. Some babies develop a weak or altered cry. In progressive cases, the infant may develop flaccid paralysis; a “floppy head” is typical. In severe cases, there may be respiratory arrest and death. The symptoms and severity of this disease vary considerably in different babies.

Intestinal botulism in adults

The initial symptoms of intestinal botulism in adults may include lassitude, weakness and vertigo. As the disease progresses, patients may experience double vision and have progressive difficulty speaking and swallowing. Other symptoms may include dyspnea, general muscle weakness, abdominal distention and constipation.

Communicability

No person–to–person transmission has been seen.

Diagnostic Tests

Botulism can tentatively diagnosed by the clinical signs and the exclusion of other neurologic diseases. The definitive diagnosis relies on identifying the toxin in feces, blood, vomitus, gastric aspirates, respiratory secretions or food samples. Feces are usually the most reliable clinical sample in foodborne or infant botulism; the toxin may be found for days or weeks in foodborne cases. Botulinum toxin is rarely found in the blood in adults but is occasionally detected in infants. The toxin can be identified by mouse inoculation studies (the mouse neutralization test), ELISAs or electrochemiluminescent (ECL) tests. Botulinum toxins can be typed with neutralization tests in mice. Serology is not useful for diagnosis, as small amounts of toxin are involved and survivors rarely develop antibodies.

C. botulinum can often be cultured from the feces in infant botulism or the wound in wound botulism. In foodborne cases, the food is usually cultured as well as tested for the toxin. C. botulinum is an anaerobic, Gram positive, spore–forming rod. On egg yolk medium, toxin–producing colonies usually display surface iridescence that extends beyond the colony. The iridescent zone around the colony is usually larger for C, D and E toxins.

Treatment and Vaccination

Supportive treatment, with respiratory support if necessary, is the cornerstone of treatment. Botulinum antitoxin, given early, may prevent the disease from progressing and decrease the duration of symptoms. In

foodborne illness, the amount of toxin in the gastrointestinal tract can be reduced with stomach lavage and enemas. Antibiotics and debridement are used in cases of wound botulism. Antibiotics are also used occasionally in foodborne cases, but are not generally recommended in infant botulism as they may change the intestinal flora. Investigational vaccines may be available for humans who have a high risk of exposure.

Morbidity and Mortality

Outbreaks of botulism can occur worldwide. Approximately 10 to 30 outbreaks are seen annually in the United States. In 1999, 107 cases of infant botulism, 26 cases of foodborne botulism and 41 cases of wound botulism were reported in the United States.

The death rate is high in untreated cases, but has been decreasing with improvements in supportive care. Before 1950, the mortality rate was 60%; currently, it is less than 5%. Recovery may be slow and can take several months or longer. In some cases, survivors report fatigue and shortness of breath for years.

Botulinum toxins are known to have been weaponized by several countries and terrorist groups.

Infections in Animals

Species Affected

Many species of mammals and birds, as well as some fish, can be affected by botulism. Clinical disease is seen most often in wildfowl, poultry, mink, cattle, sheep, horses and some species of fish. Dogs, cats and pigs are resistant; botulism is seen occasionally in dogs and pigs but has not been reported from cats.

Incubation Period

The incubation period can be 2 hours to 2 weeks; in most cases, the symptoms appear after 12 to 24 hours. Mink are often found dead within 24 hours of ingesting the toxin.

Clinical Signs

Botulism is characterized by progressive motor paralysis. Typical clinical signs may include muscle paralysis, difficulty chewing and swallowing, visual disturbances and generalized weakness. Death usually results from paralysis of the respiratory or cardiac muscles.

Ruminants

In cattle, the symptoms may include drooling, restlessness, incoordination, urine retention, dysphagia and sternal recumbency. Lateral recumbent animals are usually very close to death. In sheep, the symptoms may include drooling, a serous nasal discharge, stiffness and incoordination. Abdominal respiration may be observed and the tail may switch on the side. As the disease progresses, the limbs may become paralyzed and death may occur.

Horses

The clinical signs in horses are similar to cattle. The symptoms may include restlessness, knuckling, incoordination, paralysis of the tongue, drooling and sternal recumbency. The muscle paralysis is progressive; it usually begins at the hindquarters and gradually moves to the front limbs, head and neck.

The shaker foal syndrome is usually seen in animals less than 4 weeks old. The most characteristic signs are a stilted gait, muscle tremors and the inability to stand for more than 4 to 5 minutes. Other symptoms may include dysphagia, constipation, mydriasis and frequent urination. In the later stages, foals usually develop tachycardia and dyspnea. Death generally occurs 24 to 72 hours after the initial symptoms and results from respiratory paralysis. Some foals are found dead without other clinical signs.

Pigs

Pigs are relatively resistant to botulism. Reported symptoms include anorexia, refusal to drink, vomiting, pupillary dilation and muscle paralysis.

Foxes and Mink

During outbreaks of botulism, many animals are typically found dead, while others have various degrees of paralysis and dyspnea. The clinical picture is similar in commercially raised foxes.

Birds

In poultry and wild birds, flaccid paralysis is usually seen in the legs, wings, neck and eyelids. Wildfowl with paralyzed necks may drown. Broiler chickens with the toxicoinfectious form may also have diarrhea with excess urates.

Communicability

Botulism is not communicable by casual contact but, in some cases, tissues from dead animals can be toxic if ingested by other animals.

Diagnostic Tests

Botulism can be difficult to diagnose, as the toxin is not always found in clinical samples or the feed. Diagnosis is often a matter of excluding other diseases. A definitive diagnosis can be made if botulinum toxin is identified in the feed, stomach or intestinal contents, vomitus or feces. The toxin is occasionally found in the blood in peracute cases. Botulinum toxin can be detected by a variety of techniques, including enzyme–linked immunosorbent assays (ELISAs), electrochemiluminescent (ECL) tests and mouse inoculation or feeding trials. The toxins can be typed with neutralization tests in mice.

In toxicoinfectious botulism, the organism can be cultured from tissues. C. botulinum is an anaerobic, Gram positive, spore–forming rod. On egg yolk medium, toxin–producing colonies usually display surface iridescence that extends beyond the colony. The iridescent zone around the colony is usually larger for C, D and E toxins.

Treatment and Vaccination

The treatment is usually supportive and may include gastric lavage to remove some of the toxin. Botulinum antitoxin is sometimes used in animals; the success rate may depend on the type of toxin causing the disease and the species of animal. Type C antitoxins have been effective in some outbreaks in birds and mink. There are also some reports of success with guanidine hydrochloride. Antibiotics are used in the toxicoinfectious form, but are not always successful in birds.

In endemic areas, vaccines can be used in horses, cattle, sheep, goats, mink and pheasants. In chickens, they may not be cost–effective.

Morbidity and Mortality

Botulism is common in wild waterfowl; an estimated 10 to 50 thousand wild birds are killed annually. In some large outbreaks, a million or more birds may die. Ducks appear to be affected most often. Botulism also affects commercially raised poultry. In chickens, the mortality rate varies from a few birds to 40% of the flock. Some affected birds may recover without treatment.

Botulism seems to be relatively uncommon in most domestic mammals; however, in some parts of the world, epidemics with up to 65% morbidity are seen in cattle. The prognosis is poor in large animals that are recumbent. In cattle, death generally occurs within 6 to 72 hours after sternal recumbency. Most dogs with botulism recover within 2 weeks.

Post–Mortem Lesions

There are no pathognomonic lesions; the lesions are usually the result of general muscle paralysis. Respiratory paralysis may cause nonspecific signs in the lungs. In shaker foal syndrome, the most consist lesions are excess pericardial fluid with strands of fibrin, pulmonary edema and congestion. Foreign material in the fore–stomachs or stomach may suggest botulism.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Bacteriological Analytical Manual Online
http://www.cfsan.fda.gov/~ebam/bam–toc.html

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/botulism_t.htm

Manual on meat inspection for developing countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

Material Safety Data Sheets–Canadian Laboratory Center for Disease Control http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology
http://www.gsbs.utmb.edu/microbook

The Merck Manual
http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's *Medical Management of Biological Casualties Handbook*
http://www.vnh.org/BIOCASU/toc.html

U.S. FDA Foodborne Pathogenic Microorganisms and Natural Toxins Handbook (Bad Bug Book)
http://vm.cfsan.fda.gov/~mow/intro.html

References

"Botulinum." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 10 Dec 2002 <http://www.vnh.org/BIOCASU/17.html>.

"Botulism." *Centers for Disease Control and Prevention (CDC)*, June 2002. 10 Dec 2002 <http://www.cdc.gov/ncidod/dbmd/diseaseinfo/botulism_t.htm>.

"Botulism." In *Control of Communicable Diseases Manual*, 17th ed. Edited by J. Chin. Washington, D.C.: American Public Health Association, 2000, pp. 70–75.

"Botulism." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 442–444; 916 1315; 1362; 1969–70.

"Clostridium botulinum." In *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*. U.S. Food & Drug Administration, Center for Food Safety & Applied Nutrition, Feb 2002. 12 Dec 2002 <http://www.cfsan.fda.gov/~mow/chap2.html>

Herenda, D., P.G. Chambers, A. Ettriqui, P. Seneviratna, and T.J.P. da Silva. "Botulism."

In *Manual on meat inspection for developing countries*. FAO Animal Production and Health Paper 119. 1994 Publishing and Multimedia Service, Information Division, FAO, 12 Dec 2002 <http://www.fao.org/docrep/003/t0756e/T0756E03.htm#ch3.3.2>.

"Material Safety Data Sheet –*Clostridium botulinum*." January 2001 *Canadian Laboratory Centre for Disease Control*. 10 Dec 2002 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds35e.html>.

Solomon H.M. and T. Lilly, Jr. "Clostridium botulinum." In *Bacteriological Analytical Manual Online,* 8th ed. U.S. Food and Drug Administration, January 2001. 12 Dec 2002 <http://vm.cfsan.fda.gov/~ebam/bam–17.html>.

Wells C.L. and T.D. Wilkins. "Clostridia: sporeforming anaerobic bacilli." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 10 Dec 2002 <http://www.gsbs.utmb.edu/microbook/ch018.htm>.

Weber, J.T., C.L. Hatheway and M.E. St. Louis. "Botulism" In *Infectious Diseases,* 5th ed. Edited by P.D. Hoeprich, M.C. Jordan, and A.R. Ronald. Philadelphia: J. B. Lippincott Company, 1994, pp. 1185–1194.

Brucellosis

Malta Fever, Mediterranean Fever, Undulant Fever
Enzootic Abortion, Contagious Abortion, Bang's Disease

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Brucellosis results from infection by various species of *Brucella*, a Gram negative, facultative intracellular rod in the family Brucellaceae. Six species occur in humans and animals: *Brucella abortus*, *B. melitensis*, *B. suis*, *B. ovis*, *B. canis* and *B. neotomae*. *B. abortus* usually causes brucellosis in cattle, bison and water buffalo. *B. melitensis* is the most important species in sheep and goats, and *B. suis* in pigs. *B. ovis* can cause infertility in rams. *B. neotomae* is found in American wood rats. In humans, brucellosis can be caused by *B. abortus*, *B. melitensis*, *B. suis* and, rarely, *B. canis*. The vaccines for *B. abortus* and *B. melitensis* are also pathogenic for humans.

Seven biovars have been identified for *B. abortus,* three for *B. melitensis* and five for *B. suis*. *B. suis* biotype 4 was formerly known as *B. rangiferi*.

Geographic Distribution

Brucellosis is found worldwide but is well controlled in most developed countries. Clinical disease is still common in Africa, the Middle East, Central and Southeast Asia, South America and some Mediterranean countries.

Brucella species vary in their geographic distribution. *B. melitensis* is particularly common in Latin America, central Asia, the Mediterranean, and around the Arabian Gulf. This species does not seem to occur in northern Europe, Southeast Asia, Australia or New Zealand. It is rare in the United States. *B. ovis* is seen in Australia, New Zealand and many other sheep-raising regions, including the United States. *B. suis* can be found worldwide, but the infection rate is high only in parts of South America and Southeast Asia, and in feral pigs in Australia and the southeastern United States. *B. abortus* has been eradicated from Japan, Canada, northern Europe, Australia and New Zealand. In humans, brucellosis is rare in Europe, Canada and United States but occurs regularly in the Middle East, the Mediterranean, Mexico and Central America.

Transmission

Among animals, *Brucella* is usually transmitted by contact with the placenta, fetus, fetal fluids and vaginal discharges from infected animals. Animals are infectious after either an abortion or full term parturition. Bacteria can also be found in the blood, urine, milk and semen; shedding in milk and semen can be prolonged or lifelong. Infection occurs by ingestion and through mucous membranes, broken skin and possibly intact skin. The mammary gland can be infected by direct contact; in cattle, the udder can be colonized by *B. abortus*, *B. melitensis* or *B. suis* on the hands of farm workers. *B. suis*, *B. ovis* and *B. canis* can be spread venereally; venereal transmission of *B. abortus* can occur but is rare. Some *Brucella* species can be transmitted vertically.

Humans become infected by ingestion or through the mucous membranes and breaks in the skin. Brucellosis is sometimes spread by raw milk and unpasteurized cheese. In abattoirs and in the laboratory, *Brucella* can probably be transmitted by aerosols. *B. canis* is rare in humans; infections are thought to occur only after frequent close contact.

Brucella can be spread on fomites. In conditions of high humidity, low temperatures and no sunlight, these organisms can remain viable for several months in water, aborted fetuses, manure, wool, hay, equipment and clothes. *Brucella* is destroyed by several hours of exposure to direct sunlight.

Disinfection

Brucella is susceptible to 1% sodium hypochlorite, 70% ethanol, iodine/alcohol solutions, glutaraldehyde and formaldehyde. Bacteria can also be inactivated by moist heat (121°C for a minimum of 15 min) or dry heat (160 to 170°C for a minimum of an hour).

Infections in Humans

Incubation Period

The incubation period is difficult to determine in humans but has been estimated at 5 days to several months. Most infections seem to become apparent after 2 to 4 weeks. Aerosolization of bacteria in biological weapons could result in a shorter incubation period.

Clinical Signs

Asymptomatic infections are common in humans. In symptomatic cases, the disease is extremely variable and the clinical signs may appear insidiously or abruptly. Some cases of brucellosis resemble influenza; the symptoms may include fever, headache, generalized weakness, malaise, sweating, fatigue and severe limb or back pains. Coughing and pleuritic chest pain are occasionally seen. Gastrointestinal signs, including anorexia, nausea, vomiting, diarrhea and constipation occur frequently in adults but less often in children. Irritability, insomnia, mental depression and emotional instability sometimes develop.

In many patients, the symptoms last for 2 to 4 weeks and are followed by spontaneous recovery. Others develop an intermittent fever, with symptoms recurring and receding at 2- to 14- day intervals. Most people with this undulant form recover completely in 3 to 12 months. A few patients become chronically ill, with symptoms of chronic fatigue, depressive episodes and arthritis. Relapses can be seen months after the initial symptoms, even in successfully treated cases. Hypersensitivity reactions can mimic the symptoms of brucellosis.

Occasional complications include arthritis, endocarditis, granulomatous hepatitis, meningitis, uveitis, orchitis, cholecystitis, osteomyelitis and other bone lesions. Rare cases of encephalitis, peripheral neuropathy, radiculoneuropathy and meningovascular syndromes have also been reported.

Communicability

Brucellosis is not usually transmitted from person to person. Rarely, bacteria have been spread in tissue transplants and by sexual contact.

Diagnostic Tests

A presumptive diagnosis can be made by identifying the characteristic organisms with a modified acid-fast stain. The definitive diagnosis is by culture or serology. PCR techniques may also be available. *Brucella* species can sometimes be isolated from the blood early in the infection; bone marrow is often positive at this stage. Occasionally, bacteria can be recovered from the cerebrospinal fluid, urine or tissues.

In humans, most infections are diagnosed by serology. Serologic tests include serum agglutination, a modified Coombs' (antiglobulin) technique, ELISAs and immunoblotting (Western blotting). Serologic diagnosis is complicated by previous exposures and other factors. Chronic brucellosis can be extremely difficult to diagnose, if the serologic results are equivocal and the organism cannot be cultured.

Treatment and Vaccination

Antibiotics are usually the mainstay of treatment; long-term treatment may be required. Some forms of localized disease, such as endocarditis, may require surgery. Vaccines have not been developed for humans.

Morbidity and Mortality

Brucellosis is usually an occupational disease; most cases occur in abattoir workers, veterinarians, hunters, farmers and livestock producers. In rural areas, children are sometimes infected after drinking raw milk or eating unpasteurized cheese. Human brucellosis is rare in the United States; the annual incidence is 0.5 cases per 100,000 persons. The incidence is much higher in some other parts of the world, particularly in southwest Asia; in Kuwait, the annual incidence is up to 128 cases per 100,000 persons.

Many infections are asymptomatic but symptomatic infections can be prolonged, with slow recovery and a small possibility of complications. Increased numbers of symptomatic infections could be seen after a biological attack with aerosolized bacteria. The mortality rate is low; in untreated persons, estimates of the case fatality rate vary from less than 2% to 5%. Deaths are usually caused by endocarditis or meningitis.

Infections in Animals

Species Affected

Most species of *Brucella* are associated with a limited number of hosts, but infections can occur in other species, particularly when they are kept in close contact. *Brucella abortus* is found in cattle, bison and water buffalo and occasionally in sheep, goats and dogs. *B. melitensis* is the most important cause of brucellosis in sheep and goats. It occasionally occurs in cattle and dogs. *B. suis* infects domestic and feral pigs. Some biovars can infect reindeer, caribou, hares, mice, Arctic foxes, wolves, rodents and occasionally cattle and dogs. *B. ovis* is seen in sheep, *B. canis* in dogs and *B. neotomae* in American wood rats. Horses can develop fistulous withers or poll evil from *Brucella abortus* and occasionally *B. suis*. *Brucella* species have also been found in deer, bison, elk, coyotes, camels, moose, hares, chickens and desert rats.

Incubation Period

Systemic signs are not generally seen after infection. The period between infection and reproductive signs is

variable. In cattle, abortions and stillbirths usually occur 2 weeks to five months after infection.

Clinical Signs

Brucellosis in cattle

In cattle, *B. abortus* causes abortions, stillbirths and weak calves; abortions usually occur during the second half of gestation. The placenta may be retained and lactation may be decreased. Testicular abscesses are sometimes seen in bulls. Arthritis can develop after long-term infections. Systemic signs do not usually occur.

Brucellosis in sheep and goats

In sheep and goats, *B. melitensis* can cause abortion, retained placenta, orchitis and epididymitis. Abortions usually occur late in gestation in sheep and during the fourth month of gestation in goats. In goats, mastitis and lameness may be seen. Arthritis is rare in sheep.

B. ovis affects sheep but not goats. This organism can cause epididymitis, orchitis and impaired fertility in rams. Initially, only poor quality semen may be seen; later, lesions may be palpable in the epididymis and scrotum. The testes may atrophy permanently. Abortions, placentitis and perinatal mortality can be seen but are uncommon. Systemic signs are rare.

Brucellosis in pigs

In pigs, the most common symptom is abortion, which can occur at any time during gestation, and weak or stillborn piglets. Vaginal discharge is often minimal and the abortions may be mistaken for infertility. Temporary or permanent orchitis can be seen in boars. Boars can also excrete *B. suis* asymptomatically in the semen and sterility may be the only sign of infection. Swollen joints and tendon sheaths or lameness can occur in both sexes. Less common signs include posterior paralysis, metritis, and abscesses in other parts of the body. Although some pigs recover, others remain permanently infected. Fertility can be permanently impaired.

Brucellosis in horses

In horses, *B. abortus* and occasionally *B. suis* can cause inflammation of the supraspinous or supra-atlantal bursa; this syndrome is known, respectively, as fistulous withers or poll evil. The bursal sac becomes distended by a clear, viscous, straw-colored exudate and develops a thickened wall. It can rupture, leading to secondary inflammation. In chronic cases, nearby ligaments and the dorsal vertebral spines may become necrotic. *Brucella*-associated abortions are rare in horses.

Brucellosis in dogs

B. canis causes abortions, stillbirths and infertility in dogs. Most infections are seen in kennels. Abortions usually occur during the last trimester and are followed by a prolonged vaginal discharge. Infected dogs may have lymphadenitis, epididymitis, periorchitis and prostatitis. Fever is not usually seen.

Communicability

Yes. Bacteria are present in the placenta, fetal fluids, fetus, vaginal discharges, milk, semen and urine. Infectious bacteria are also found in the bursa of horses with poll evil or fistulous withers. Some animals, particularly ruminants, can shed bacteria long-term or lifelong.

Diagnostic Tests

Brucellosis can be diagnosed by culture, serology or other tests. Some serologic tests are not useful in some hosts or for some species of *Brucella*.

Microscopic examination

A presumptive diagnosis can be made if the characteristic organisms are found in abortion products, vaginal discharges, milk, semen or various tissues by modified acid-fast staining. *Brucella* is an aerobic, nonmotile, Gram negative coccobacillus or short rod. Bacteria are usually found singly, but are occasionally seen in pairs or small groups. Direct examination may not detect the small numbers of organisms present in milk and dairy products.

Culture

Brucella species can be recovered from numerous tissues, particularly fetal membranes, vaginal secretions, milk, semen, arthritis or hygroma fluids, and the stomach contents, spleen and lung from aborted fetuses. In carcasses, bacteria can sometimes be isolated from the lymph nodes, spleen, uterus, udder, testis, epididymis, joint exudate, abscesses and other tissues. Repeated sampling of the semen may be necessary in *B. ovis* infections, as this organism is shed intermittently. Blood can be cultured from dogs; this species can be bacteremic for as long as 18 months after infection.

A wide variety of media can be used for culture; suitable media include Trypticase soy agar, modified Thayer-Martin medium, Farrell's medium, serum dextrose agar, glycerol dextrose agar and Castañeda's medium. In a four-day old culture, colonies of the smooth form viewed through a transparent medium are a pale honey color, 1-2 mm in diameter, translucent and round, with smooth margins. The colonies are convex and pearly white when seen from above. In the rough form, the colonies are much less transparent and have a more granular, dull, matte white to brown surface. In nature, *Brucella abortus*, *B. melitensis*, *B. suis* and *B. neotomae* usually occur in the smooth form; *B. ovis* and *B. canis* are found in the rough form. Identification to the genus level is by biochemical tests and slide agglutination. The species and

biovar can be identified by phage lysis and cultural, biochemical and serological characteristics.

Serology

Brucellosis is often diagnosed by serology. In cattle, agglutination tests are used to detect antibodies in serum, milk, whey and semen. The most commonly used tests are the buffered *Brucella* antigen tests (BBAT), also known as the card and plate agglutination tests. Tube agglutination tests may also be used. An enzyme-linked immunosorbent assay (ELISA) is available for milk or serum. The milk ring test can be used to screen bulk milk samples for *B. abortus*. Other, less commonly used, serologic tests include complement fixation, rivanol precipitation and acidified antigen procedures. Fluorescence polarization tests are being developed.

In sheep and goats, *B. melitensis* can be diagnosed with BBAT or complement fixation. ELISAs are being developed. The bulk milk ring test is not used in small ruminants. *B. ovis* infections can be diagnosed by ELISA, complement fixation, hemagglutination inhibition, indirect agglutination and gel diffusion tests.

The tube or slide agglutination and gel diffusion tests are generally used in dogs. Nonspecific agglutination sometimes occurs but can be eliminated by pretreatment with 2-mercaptoethanol.

Serology is less reliable in pigs. Conventional serologic tests can misdiagnose *B. suis* infections in individual pigs; these tests are considered to be more reliable for a herd diagnosis. The BBATs are used most often; complement fixation or other serum agglutination tests may also be available. ELISA techniques and fluorescence polarization assays have been developed and may be more effective than other serologic tests.

Other tests

Immunofluorescent techniques can detect *B. abortus* in the placenta and fetus or *B. ovis* in the semen. A brucellin allergic skin test is sometimes used to test pigs for *B. suis* or unvaccinated sheep and goats for *B. melitensis*. This assay is generally a herd test. Polymerase chain reaction (PCR) techniques have also been developed for some species.

Treatment and Vaccination

There is no practical treatment for infected cattle or pigs, but long-term antibiotic treatment is sometimes successful for *B. canis* infections in dogs. Antibiotics can eliminate *B. ovis* infections in valuable rams but the fertility may remain poor. In horses with fistulous withers or poll evil, the infected bursa may need to be surgically removed.

Commercial vaccines are available for cattle, sheep and goats. A *B. ovis* vaccine is manufactured in New Zealand and some other counties but is not available in the United States. Successful vaccines have been difficult to develop for pigs; this species is generally not vaccinated except in China. No vaccines are made for dogs. Vaccines have not been successful in preventing fistulous withers or poll evil in horses.

Morbidity and Mortality

Morbidity can be high in naïve animals. In cattle, *B. abortus* can spread rapidly in an unvaccinated, naïve herd; 80% of cattle in late gestation may abort. In dogs, up to 75% fewer puppies may be weaned from affected kennels. In pigs, the abortion rate is 0 to 80%. Ruminants usually abort only during their first gestation, but abortions can occur repeatedly in affected dogs. Fertility can be permanently impaired after infections with some species of *Brucella*. Deaths are not usually seen in adult animals.

Post-Mortem Lesions

In ruminants, the fetus may be autolyzed, normal or have evidence of bronchopneumonia. In cattle, acute or chronic placentitis is sometimes seen. The cotyledons may be red, yellow, normal or necrotic. The intercotyledonary region is typically leathery, with a wet appearance and focal thickening. Placentitis, with edema and necrosis of the cotyledons and a thickened and leathery intercotyledonary region, can also be seen in sheep infected with *B. melitensis*. The placenta is usually normal in goats. Fetal and placental lesions are rare in pigs infected with *B. suis*, but the fetus may be autolyzed.

At slaughter, granulomatous inflammatory lesions may be found in the reproductive tract, mammary gland, supramammary lymph nodes and joints of adult animals.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr-bin/aphb/ahsq?dislist=alpha

Brucellosis in Sheep and Goats (Brucella melitensis)
European Commission Health and Consumer Protection Directorate General
http://europa.eu.int/comm/food/fs/sc/scah/out59_en.pdf

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_t.htm

FAO Manual on meat inspection for developing countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

Material Safety Data Sheets–
Canadian Laboratory Center for Disease Control
http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/

index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines

http://www.oie.int/eng/normes/mmanual/a_summry.htm

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

References

Alton G.G. and J.R.L. Forsyth. "*Brucella*." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 15 Dec 2002 <http://www.gsbs.utmb.edu/microbook/ch028.htm>.

"Bacterial infections caused by Gram-negative bacilli. Enterobacteriaceae." In *The Merck Manual*, 17th ed. Edited by M.H. Beers and R. Berkow. Whitehouse Station, NJ: Merck and Co., 1999. 8 Nov 2002 <http://www.merck.com/pubs/mmanual/section13/chapter157/157d.htm>.

"Brucellosis (*Brucella melitensis*, *abortus*, *suis*, and *canis*). *Centers for Disease Control and Prevention*, June 2002. 16 Dec 2002 <http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_t.htm>.

"Brucellosis." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 16 Dec 2002 <http://www.vnh.org/BIOCASU/7.html>.

"Brucellosis." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 991; 993; 994; 996; 998-1002; 1043.

"Brucellosis in Sheep and Goats (*Brucella melitensis*)." July 2001 European Commission Health and Consumer Protection Directorate General. 17 Dec 2002 <http://europa.eu.int/comm/food/fs/sc/scah/out59_en.pdf>.

"Caprine and Ovine Brucellosis (excluding *B. ovis* infection)." In *Manual of Standards for Diagnostic Tests and Vaccines.* Paris: Office International des Epizooties, 2000. 16 Dec 2002 <http://www.oie.int/eng/normes/mmanual/A_00063.htm>.

"Control of Communicable Diseases." Edited by J. Chin. American Public Health Association, 2000, pp. 75-78.

"Fistulous withers and poll evil." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, p. 762.

Herenda, D., P.G. Chambers, A. Ettriqui, P. Seneviratna, and T.J.P. da Silva. "Brucellosis." In *Manual on meat inspection for developing countries.* FAO Animal Production and Health Paper 119. 1994 Publishing and Multimedia Service, Information Division, FAO, 17 Dec 2002 <http://www.fao.org/docrep/003/t0756e/T0756E03.htm#ch3.3.7>.

"Material Safety Data Sheet –*Brucella* spp." *Canadian Laboratory Centre for Disease Control*, January 2001. 16 Dec 2002 <http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/msds23e.html>.

Plommet M., Diaz R. and J-M. Verger. "Brucellosis." In *Zoonoses*. Edited by S.R. Palmer, E.J.L. Soulsby and D.I.H Simpson. New York: Oxford University Press, 1998, pp. 23-35.

"Porcine Brucellosis." In *Manual of Standards for Diagnostic Tests and Vaccines.* Paris: Office International des Epizooties, 2000. 16 Dec 2002 <http://www.oie.int/eng/normes/mmanual/A_00083.htm>.

Eastern Equine Encephalomyelitis, Western Equine Encephalomyelitis and Venezuelan Equine Encephalomyelitis

"Sleeping Sickness"

Eastern Equine Encephalomyelitis –EEE, Eastern equine encephalitis, Eastern encephalitis

Western Equine Encephalomyelitis –WEE, Western equine encephalitis

Venezuelan Equine Encephalomyelitis –VEE, VE, Peste loca, Venezuelan equine encephalitis, Venezuelan encepha - litis, Venezuelan equine fever

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Eastern, Western and Venezuelan equine encephalomyelitis result from infection by the respectively named viruses in the genus *Alphavirus* (family Togaviridae). In the human literature, the disease is usually called Eastern, Western or Venezuelan equine encephalitis.

Eastern Equine Encephalomyelitis Virus

There are two variants of the Eastern equine encephalomyelitis (EEE) virus. The virus found in North America is more pathogenic than the variant that occurs in South and Central America. The Eastern equine encephalitis virus can cause disease in humans, horses and some species of birds.

Western Equine Encephalomyelitis Viruses

The Western equine encephalomyelitis (WEE) virus group includes the Western equine encephalitis (WEE), Sindbis, Ft. Morgan, Aura and Y 61–33 viruses. The Western equine encephalitis virus can cause disease in humans, horses and some species of birds. A related virus, the Highlands J virus, is sometimes isolated in the eastern United States. The Highlands J virus can cause disease in turkeys. It has also been linked to a single case of encephalitis in a horse.

Venezuelan Equine Encephalomyelitis Viruses

The Venezuelan equine encephalomyelitis (VEE) complex contains at least 8 viral subtypes; these viruses are divided into epizootic and enzootic groups. The epizootic subtypes are responsible for most epidemics. They are highly pathogenic for horses and also cause illness in humans. Enzootic (sylvatic) subtypes are generally found in limited geographic areas, where they occur in natural cycles between rodents and mosquitoes. The enzootic subtypes can cause human disease. They are usually non-pathogenic for horses; however, in 1993 an enzootic variant was responsible for an outbreak of VEE among horses in Mexico.

Geographic Distribution

The Western, Eastern and Venezuelan encephalomyelitis viruses are found in North, Central and South America. The WEE viruses occur in western Canada, Mexico, parts of South America, and west of the Mississippi in the United States. The EEE virus is found in eastern Canada, all states east of the Mississippi, Arkansas, Minnesota, South Dakota and Texas. It also occurs in the Caribbean and regions of Central and South America, particularly along the Gulf coast. VEE viruses are endemic in South and Central America and Trinidad. Enzootic subtypes of VEE are also found in Florida, the Rocky Mountains and northern plains of the United States. Most epidemics of VEE occur in northern and western South America, but some may spread into adjacent countries, including the United States.

Transmission

Eastern and Western Equine Encephalomyelitis

The Eastern and Western encephalomyelitis viruses are transmitted mainly by mosquitoes. Normally, these two viruses cycle between birds and mosquitoes. Humans and horses are incidental, dead end hosts.

The EEE virus can be isolated from 27 species of mosquitoes in the United States. *Culiseta melanura*, a mosquito that primarily feeds on birds, is the most important vector in the enzootic cycle. During some years, the virus is spread to mammalian hosts by bridge vectors (mosquitoes that feed on both birds and mammals) such as *Coquilletidia perturbans*, *Aedes canadensis*, *Aedes sollicitans*, *Aedes vexans* and *Culex nigripalpus*. WEE cycles between passerine birds and culicine mosquitoes. *Culex tarsalis* appears to be the most important vector; other significant vectors include *Aedes melanimon*, *Aedes dorsalis* and *Aedes campestris*. The EEE and WEE viruses may be transmitted vertically in mosquitoes.

In birds, EEE and WEE are occasionally spread by non–arthropod–borne routes. During outbreaks of disease in game birds, infections are introduced by mosquitoes but spread in the flock mainly by feather picking and cannibalism. EEE and WEE viruses do not survive outside the host.

Venezuelan Equine Encephalomyelitis

The Venezuelan equine encephalomyelitis viruses are also spread mainly by mosquitoes. The enzootic subtypes of VEE cycle between rodents and mosquitoes, mainly *Culex* species. Birds may also be involved in some cycles. Humans and horses are incidental hosts.

The natural host for the epizootic subtypes, between epidemics, is unknown. Horses infected with the epizootic subtypes can infect mosquitoes and are the main amplifiers for VEE during epidemics. Other mammals, including cattle, pigs and dogs, can be infected but do not usually become ill or spread the virus. Many different species of mosquitoes and other hematogenous insects can transmit epizootic VEE. Efficient vectors include arthropods in the genera *Aedes*, *Anopheles*, *Culex*, *Deinocerites*, *Mansonia*, *Haemogogus*, *Sabethes* and *Psorophora*.

In some cases, humans have also developed VEE after being exposed to debris from the cages of infected laboratory rodents. Person–to–person transmission has not been reported; however, the VEE virus can be found in pharyngeal secretions in humans and is stable when aerosolized. The virus can also occur in dried blood and exudates.

Disinfection

EEE and WEE viruses do not persist in the environment but the VEE virus may be found in dried blood and exudates. VEE, EEE and WEE are susceptible to many disinfectants including 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde and formaldehyde. They can also be destroyed by moist or dry heat, as well as drying.

Infections in Humans

Incubation Period

In humans, the incubation period is usually 1 to 6 days for VEE and 4 to 15 days for WEE and EEE.

Clinical Signs

Eastern and Western Equine Encephalitis

Eastern equine encephalitis usually begins abruptly, with fever, myalgia and headache and sometimes nausea and vomiting. This prodrome is often followed by neurologic signs; the symptoms may include confusion, focal neurologic deficits, somnolence, neck stiffness, stupor, disorientation, coma, tremors, seizures and paralysis. Abdominal pain, diarrhea and a sore throat can also occur. The mortality rate for EEE is high.

Western equine encephalitis resembles EEE but is usually asymptomatic or mild in adults, with nonspecific signs of illness and few deaths. The symptoms usually appear abruptly and may include fever, headache, nausea, vomiting, anorexia and malaise. Many adults do not develop other symptoms. In more severe cases, neurologic symptoms, similar to those seen in EEE, can develop. WEE can be severe in children, particularly infants under a year of age.

Venezuelan Equine Encephalitis

In humans, VEE is usually an acute, often mild, systemic illness. The clinical signs may include fever, generalized malaise, severe headache, photophobia and myalgia, particularly in the legs and lum*bos*acral region. These symptoms usually last for 24 to 72 hours and may be followed by a cough, sore throat, nausea, vomiting and diarrhea. The disease usually lasts 1 to 2 weeks. In pregnant women, VEE can affect the fetus; fetal encephalitis, placental damage, abortion or severe congenital neurologic anomalies may be seen.

Encephalitis usually develops in 4% of children and less than 1% of adults. In mild cases, the symptoms may include lethargy, somnolence, or mild confusion. Severe infections are characterized by seizures, ataxia, paralysis or coma. An increased incidence of encephalitis would be expected after a biological attack with aerosolized viruses.

Communicability

WEE and EEE viruses are not found in the blood or cerebrospinal fluid after the symptoms appear, and only low titers develop during the viremic phase. These viruses do not seem to be spread directly from person to person. Humans do not transmit EEE or WEE viruses to mosquitoes.

Person–to–person transmission is theoretically possible for VEE, but has not been reported in natural cases. Humans with VEE can infect mosquitoes for approximately 72 hours.

Diagnostic Tests

Eastern, Western and Venezuelan equine encephalitis can be diagnosed by virus isolation, serology or other tests. In humans, VEE virus can be isolated from blood, cerebrospinal fluid or throat swabs. Serology is also useful; a rise in titer or the presence of specific IgM is diagnostic. A variety of serologic tests may be available, including virus neutralization, ELISA, hemagglutination inhibition and complement fixation. Indirect immunofluorescence assays have been developed for VEE. Polymerase chain reaction (PCR) or immunohistochemistry may be available at some laboratories.

During the febrile stage of the illness, antigen–capture ELISAs can often detect VEE antigens in the blood. This test is generally not useful during the encephalitic stage. PCR assays may also be available.

Treatment and Vaccination

Treatment consists of supportive care. Investigational VEE, EEE and WEE vaccines may be available for humans at high risk of infection. The VEE vaccine may not be effective for all of the VEE complex viruses.

Morbidity and Mortality

Eastern Equine Encephalitis

In the United States, approximately 12 to 17 cases of EEE are reported to the Centers for Disease Control and Prevention (CDC) each year. The infection rate is approximately 33% and the morbidity rate 90%. Most cases are seen in people over 55 and children younger than 15. Eastern equine encephalitis is often severe in humans. Estimates of the case fatality rate vary from 33 to 70% and permanent neurologic deficits can occur in survivors.

Western Equine Encephalitis

The annual incidence of WEE is highly variable; during an epidemic in 1941, over 3000 human cases occurred in the United States and Canada. The case–infection ratio is approximately 1:1000 in adults, 1:58 in children from 1 to 4 years old and 1:1 in infants up to a year of age. The overall mortality rate is 3 to 4%. Most infections in adults are asymptomatic or mild, without neurologic disease. Infections in children, particularly infants under one year old, can be severe. Approximately 5 to 30% of young patients have permanent neurologic damage.

Venezuelan Equine Encephalomyelitis

In natural epidemics of VEE, human cases are usually preceded by an epidemic in horses. After an attack by a biological weapon, cases would be expected simultaneously in both species or first in humans. Caution should be used in interpreting such patterns of infection, as VEE may be missed in wild or free–ranging equines.

Humans are highly susceptible to VEE; approximately 90 to 100% of exposed individuals become infected and nearly 100% of these infections are symptomatic. However, most infections are mild. Less than 1% of adults develop encephalitis and approximately 10% of these cases are fatal. The overall case fatality is less than 1%. Very young or elderly patients are more likely to develop severe infections. Encephalitis occurs in approximately 4% of children less than 15 years old; the case fatality rate in children with neurologic disease is 35%. A higher incidence of neurologic disease could be seen in adults as well as children after a biological attack with aerosolized virus; mortality rates would be expected to be correspondingly higher.

Infections in Animals

Species Affected

The equine encephalomyelitis viruses usually cause illness only in equine species and humans. These viruses can also infect a variety of other animals, often asymptomatically.

Eastern and Western Equine Encephalomyelitis

Eastern equine encephalitis virus infects horses, pigs, birds, bats, reptiles, amphibians, forest–dwelling marsupials and rodents. WEE virus can infect birds, horses and a variety of mammals. Most WEE and EEE infections in birds are asymptomatic; however, disease can be seen in chukar partridges, pheasants, psittacine birds, ratites and whooping cranes.

Venezuelan Equine Encephalomyelitis

Rodents seem to be the natural hosts for the enzootic subtypes of VEE but, in some cases, birds may also be involved. VEE virus can cause serious disease in horses, mules, burros and donkeys. Cattle, pigs and dogs can be infected asymptomatically. VEE can also infect a wide variety of laboratory animals.

Incubation Period

The incubation period for WEE or EEE is 5 to 14 days. The clinical signs of VEE are usually seen 1 to 5 days after infection.

Clinical Signs

Eastern and Western Equine Encephalomyelitis in Horses

Eastern and Western equine encephalomyelitis are very similar in horses. The initial clinical signs are usually fever, anorexia and depression. In severe cases, this prodromal stage is followed by neurologic signs; the symptoms may include involuntary muscle movements, impaired vision, aimless wandering, head pressing, circling, an inability to swallow, ataxia, paresis, paralysis and convulsions. Periods of excitement or intense pruritus can also be seen. Laterally recumbent animals may develop a characteristic “paddling” motion. Both EEE and WEE can also cause asymptomatic infections or mild disease without neurologic signs. Occasional cases of encephalitis have been seen in pigs.

Venezuelan Equine Encephalomyelitis in Horses

The enzootic subtypes usually infect horses subclinically. The epizootic subtypes can cause asymptomatic infections or two clinical syndromes. One syndrome resembles EEE and WEE; in this form, a febrile prodrome is followed by neurologic signs and sometimes diarrhea

and colic. Death can occur within hours after the onset of neurologic signs or after protracted disease. Animals that recover may have permanent neurologic signs. The second form of VEE is a generalized acute febrile disease without neurologic signs. The symptoms may include fever, weakness, depression, anorexia, colic and diarrhea.

Western and Eastern Equine Encephalitis Viruses in Birds

Western and Eastern equine encephalomyelitis virus infections are asymptomatic in most species of birds, but fatal infections can occur in some species. Most reported outbreaks have been caused by EEE. Chukar infected with the EEE virus are usually dull and listless, with ruffled feathers. The birds are typically found sitting on their hocks with the beak on the ground. In pheasants, the symptoms may include incoordination, weakness and progressive paralysis. In the late stages of the disease, the birds cannot stand but can still move their wings. Whooping cranes may develop lethargy, ataxia and paresis of the legs and neck. The EEE virus has also been isolated from psittacine birds with viral serositis.

Both EEE and WEE viruses can cause fatal hemorrhagic enteritis in ratites; the characteristic clinical signs include depression, hemorrhagic diarrhea, and vomiting of bloodstained material. Highlands J and EEE infections can also cause depression, somnolence, decreased egg production and increased mortality in turkeys.

Communicability

Birds can amplify the Western and Eastern equine encephalomyelitis viruses and are infectious for mosquitoes. Horses are dead–end hosts for these viruses. Direct transmission has been seen only between birds.

Both horses and birds infected with the VEE virus are infectious for mosquitoes. In horses, the virus can be found in bodily fluids. Some authorities suggest that transmission may be possible by direct contact or aerosols but natural transmission between horses or from horses to humans has not been seen. Humans can be infected by laboratory rodents.

Diagnostic Tests

Eastern and Western Equine Encephalomyelitis

In horses, Eastern and Western equine encephalomyelitis can be diagnosed by serology. Tests include plaque reduction neutralization (PRN), hemagglutination inhibition, antibody–capture enzyme linked immunosorbent assay (ELISA) and complement fixation. Cross–reactions may occur between EEE and WEE antibodies in the complement fixation and hemagglutination inhibition tests.

Clinical infections in birds are usually diagnosed by virus isolation. In horses, virus isolation is useful in cases of EEE; it is rarely successful in WEE. The EEE virus can usually be recovered from the brain of infected horses; other tissues such as the liver or spleen may also be positive. EEE and WEE viruses can be isolated in newborn mice, embryonating chicken eggs, newly hatched chicks or cell cultures including primary chicken or duck embryo fibroblasts, African green monkey kidney (Vero), rabbit kidney (RK–13), and baby hamster kidney (BHK–21) cells. Virus identity can be confirmed by complement fixation, immunofluorescence or plaque reduction neutralization (PRN) tests. EEE viruses can also be detected in the brain with immunohistochemistry or an antigen–capture ELISA.

Venezuelan Equine Encephalomyelitis

VEE can be diagnosed by virus isolation or serology. VEE virus can often be recovered from the blood during the febrile stage and is sometimes isolated from the brain of animals with encephalitis. Virus is also found occasionally in the pancreas or other tissues. Animals with neurologic signs are not usually viremic. VEE virus can be isolated in guinea pigs, hamsters, mice, embryonated chicken eggs or cell lines including Vero, RK–13, BHK–21 and duck or chicken embryo fibroblasts. The virus can be identified by complement fixation, hemagglutination inhibition, plaque reduction neutralization (PRN) or immunofluorescence assays. Subtypes can be characterized by immunofluorescence, differential PRN tests or nucleic acid sequencing.

VEE can also be diagnosed by serology. Serologic tests include the PRN test, complement fixation, hemagglutination inhibition and ELISAs. Cross–reactions can occur between VEE, EEE and WEE viruses in the hemagglutination inhibition test. Animals may have pre–existing antibodies to enzootic variants of VEE.

Treatment and Vaccination

Treatment consists of supportive care. Equine vaccines are available for EEE, WEE and VEE. EEE vaccines are also available for susceptible birds, but do not always prevent disease.

Morbidity and Mortality

Eastern and Western Equine Encephalomyelitis

WEE often occurs as sporadic cases of encephalitis in horses, scattered over a wide area. Clinical cases of EEE are usually more clustered. EEE is often fatal in horses; the mortality rate is 50 to 90%. WEE is more likely to be asymptomatic or mild, with mortality rates of approximately 20 to 30%. Significant morbidity and mortality can also occur in poultry, game birds and ratites. In pheasants and other susceptible species of birds, both the morbidity and mortality rates may be up to 90%. The morbidity and mortality rates for emus with hemorrhagic enteritis can be greater than 85%.

Venezuelan Equine Encephalomyelitis

Most enzootic VEE subtypes do not result in serious disease or deaths in horses. Epizootic subtypes can cause significant morbidity and mortality; the morbidity rate can be as high as 90% and the mortality rate varies from 30 to 90%.

Post–Mortem Lesions

The gross lesions are usually nonspecific. In horses with VEE, the lesions in the central nervous system vary from no lesions to extensive necrosis with hemorrhages. Necrotic foci are sometimes seen in the pancreas, liver and heart of horses with VEE. Congestion of the brain and meninges is found in some cases of EEE and WEE. Antemortem trauma can result in ecchymotic hemorrhages.

Microscopic analysis of the brain tissue is often diagnostic. The typical lesion is severe inflammation of the gray matter; neuronal degeneration, infiltration by inflammatory cells, gliosis, perivascular cuffing and hemorrhages may be seen. WEE, EEE and VEE can sometimes be differentiated by the location and pattern of the lesions in the brain.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dvbid/arbor/arbdet.htm

Manual for the Recognition of Exotic Diseases of Livestock
http://panis.spc.int/

Material Safety Data Sheets –Canadian Laboratory Center for Disease Control http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology
http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines
http://www.oie.int/eng/normes/mmanual/a_summry.htm

The Merck Manual
http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook
http://www.vnh.org/BIOCASU/toc.html

References

"Arthropod–Borne Viral Diseases." In *Control of Communicable Diseases Manual*, 17th ed. Edited by James Chin. Washington, D.C.: American Public Health Association, 2000, pp. 28–47.

"Eastern Encephalitis." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 1970–1.

"Eastern Encephalomyelitis." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 931–4.

"Equine Encephalomyelitis (Eastern and Western)." In *Manual of Standards for Diagnostic Tests and Vaccines*. Paris: Office International des Epizooties, 2000. 16 Dec 2002 <http://www.oie.int/eng/normes/mmanual/A_00071.htm>.

"Equine Viral Encephalomyelitis." In *Manual for the Recognition of Exotic Diseases of Livestock: A Reference Guide for Animal Health Staff*. Food and Agriculture Organization of the United Nations, 1998. 16 Dec 2002 <http://panis.spc.int/RefStuff/Manual/Equine/EQUINE%20VIRAL%20ENCEPH.HTML>.

"Information on Arboviral Encephalitides." *Centers for Disease Control and Prevention (CDC)*, 2001. 16 Dec 2002 <http://www.cdc.gov/ncidod/dvbid/arbor/arbdet.htm>.

Leake, Colin J. "Mosquito–Borne Arboviruses." In *Zoonoses*. Edited by S.R. Palmer, E.J.L. Soulsby and D.I.H Simpson. New York: Oxford University Press, 1998, pp. 401–413.

"Material Safety Data Sheet –Eastern equine encephalitis virus, Western equine encephalitis virus." March 2001 *Canadian Laboratory Centre for Disease Control*. 4 October 2002 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds52e.html>.

"Material Safety Data Sheet –Venezuelan equine encephalitis virus." *Canadian Laboratory Centre for Disease Control*, September 2001. 10 Dec 2002 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds162e.html>.

Nandalur M. and A.W. Urban. "Eastern Equine Encephalitis." *eMedicine*, Sept 2002. 16 Dec 2002 <http://www.*emedicine*.com/med/topic3155.htm>.

Nandalur M. and A.W. Urban. "Western Equine Encephalitis." *eMedicine*, June 2002. 16 Dec 2002 <http://www.*emedicine*.com/MED/topic3156.htm>.

Schmaljohn A.L. and D. McClain. "*Alphaviruses* (*Togaviridae*) and *Flaviviruses* (Flaviviridae)." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 16 Dec 2002 <http://www.gsbs.utmb.edu/microbook/ch054.htm>.

"Venezuelan Equine Encephalitis." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 10 Dec 2002 <http://www.vnh.org/BIOCASU/14.html>.

"Venezuelan Equine Encephalomyelitis." *USDA Animal and Plant Health Inspection Service (APHIS)*, Sept 2002. 16 Dec 2000 <http://www.aphis.usda.gov:80/oa/pubs/fsvee.html>.

"Venezuelan Equine Encephalomyelitis." In *Manual of Standards for Diagnostic Tests and Vaccines*. Paris: Office International des Epizooties, 2000. 16 Dec 2002 <http://www.oie.int/eng/normes/mmanual/A_00078.htm>.

Walton, T.E. "Venezuelan Equine Encephalomyelitis." In *Foreign Animal Diseases*. Richmond, VA: United States Animal Health Association, 1998, pp 406–414.

Glanders

Farcy, Malleus, Droes

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Glanders results from infection by *Burkholderia mallei*, a Gram negative, aerobic, nonmotile rod (family Pseudomonadaceae). This organism was formerly known as *Pseudomonas mallei* and is closely related to the agent of melioidosis, *Burkholderia pseudomallei*.

Geographic Distribution

Glanders is seen in some Middle Eastern countries, the Indian subcontinent, Southeast Asia, parts of China and Mongolia, and Africa. Sporadic cases are also seen in South America. Cross–reactions with *B. pseudomallei* may interfere with serologic estimates of the prevalence and distribution of *B. mallei*.

Transmission

Infectious organisms are found in skin exudates and respiratory secretions. Latently infected horses can also spread the disease. Transmission is usually by ingestion in horses and related species; the infection can also be spread by inhalation or through skin abrasions and the conjunctiva. Carnivores can become infected after eating contaminated meat. *B. mallei* is spread on fomites, including harnesses, grooming tools, food and water troughs. This organism can survive in room temperature water for as long as 30 days and may be able to survive for a few months in other favorable environments. It is susceptible to heat, light, drying and a variety of chemicals.

Humans can become infected after contact with sick animals or infectious materials. Transmission is typically through small wounds and abrasions in the skin; ingestion or inhalation, with invasion through the mucous membranes, is also possible. Cases are usually seen in people who handle laboratory samples or have frequent close contact with horses, mules and donkeys. Natural human infections are rare even when infection rates in horses are 5–30%. Weaponization of *B. mallei* has been attempted by some countries.

Disinfection

Burkholderia mallei is susceptible to numerous disinfectants including benzalkonium chloride, iodine, mercuric chloride in alcohol, potassium permanganate, 1% sodium hypochlorite, 70% ethanol and 2% glutaraldehyde. It is less susceptible to phenolic disinfectants. This organism can also be destroyed by heating to 55°C for 10 min or by ultraviolet irradiation.

Infections in Humans

Incubation Period

In natural infections, the incubation period is 1 to 14 days. Infections from aerosolized forms in biological weapons are expected to have an incubation period of 10–14 days.

Clinical Signs

Humans can develop four forms of disease: septicemia, pulmonary infection, acute localized infection or chronic infection. Combinations of syndromes can occur.

In the septicemic form, fever, chills, myalgia, and pleuritic chest pain develop acutely. Other symptoms may include generalized erythroderma, jaundice, photophobia, lacrimation, diarrhea and granulomatous or necrotizing lesions. Tachycardia, cervical adenopathy and mild hepatomegaly or splenomegaly may also be seen. Death usually occurs in 7 to 10 days.

The pulmonary form is characterized by symptoms of pneumonia, pulmonary abscesses and pleural infusions. A cough, fever, dyspnea and mucopurulent discharge may be seen. Skin abscesses sometimes develop after several months.

Localized infections are characterized by nodules, abscesses and ulcers in the mucous membranes, skin, lymphatic vessels and/or subcutaneous tissues. A mucopurulent, blood–tinged discharge may be seen from the mucous membranes. The

lymph nodes may be swollen. Mucosal or skin infections can disseminate; symptoms of disseminated infections include a papular or pustular rash, abscesses in the internal organs (particularly the liver and spleen) and pulmonary lesions. Disseminated infections are associated with septic shock and high mortality.

In the chronic form, multiple abscesses, nodules or ulcers can be seen in the skin, liver, spleen or muscles.

Communicability

Person to person transmission has been reported, but appears to be uncommon. Human epidemics have not been seen.

Diagnostic Tests

Glanders can be diagnosed by isolation and identification of *Burkholderia mallei*. In the septicemic form, blood cultures may be negative until just before death. *B. mallei* is a nonmotile Gram negative rod; organisms from young cultures and clinical samples are rods with bipolar staining, while bacteria from older cultures can be pleomorphic. Few bacteria may be found in clinical samples. On blood agar or Loeffler's serum agar, colonies are approximately 1 mm, white, semitranslucent and viscid. Older colonies turn yellow. On glycerin–potato media, a clear honey–like layer is seen by day 3; this eventually darkens to reddish–brown or brown. *B. mallei* can also be isolated by inoculation into guinea pigs. A polymerase chain reaction can differentiate *B. mallei* DNA from *B. pseudomallei*.

Serology is sometimes helpful; serologic tests include agglutination tests and complement fixation. High background titers can be found in normal serum and cross–reactions may occur with Burkholderia pseudomallei, the causative agent of Melioidosis Positive reactions in agglutination tests develop only after 7 to 10 days.

Treatment and Vaccination

B. mallei is variably susceptible to antibiotics. Long–term treatment or multiple drugs may be necessary. Treatment may be ineffective, particularly in cases of septicemia; the bacteria produce toxins. No vaccine is available.

Morbidity and Mortality

In most parts of the world, naturally acquired cases of glanders are rare and sporadic. Infections are typically seen in people who work with clinical samples or have frequent, close contact with horses. Human epidemics have not been seen.

The septicemic form of glanders has a high mortality rate in humans: the case fatality rate is 95% in untreated cases and more than 50% when the infection is treated. The mortality rate for localized disease is 20% when treated. The overall mortality rate is 40%.

Infections in Animals

Species Affected

The major hosts are horses, mules and donkeys. Infections can also occur in dogs, cats, goats and camels; cats may be particularly susceptible. Hamsters and guinea pigs can be infected in the laboratory.

Incubation Period

In natural infections, the incubation period varies from 6 days to many months; 2 to 6 weeks is typical. Experimental infections can result in clinical signs after 3 days.

Clinical Signs

Acute, chronic and latent forms of glanders are seen in horses, mules and donkeys.

The clinical signs in the acute form may include a high fever, cough, inspiratory dyspnea, a thick nasal discharge, and deep, rapidly spreading ulcers on the nasal mucosa. Healed ulcers become star–shaped scars. The submaxillary lymph nodes are usually swollen and painful, and the lymphatic vessels on the face may be thickened. Secondary skin infections, with nodules, ulcers and abscesses may be seen. Affected animals usually die within 1 to 2 weeks.

The chronic form develops insidiously. The symptoms may include coughing, malaise, unthriftiness, weight loss and an intermittent fever. A chronic purulent nasal discharge may be seen, often only from one nostril. Other symptoms may include ulcers and nodules on the nasal mucosa, enlarged submaxillary lymph nodes, chronic enlargement and induration of lymphatics and lymph nodes, swelling of the joints and painful edema of the legs. The skin may contain nodules, particularly on the legs, that rupture and ulcerate. This form is slowly progressive and may be fatal.

In the latent form, there may be few symptoms other than a nasal discharge and occasional labored breathing. Lesions may be found only in the lungs.

Communicability

Horses, donkeys and mules can transmit the disease to other animals and humans; nasal discharges and wound exudates are infectious. Laboratory samples are highly infectious to humans.

Natural transmission from infected animals to humans appears to be inefficient. Despite infection rates of 30% in horses in China during World War II and 5–25% in Mongolia, few or no human cases occurred.

Diagnostic Tests

Glanders can be diagnosed by bacteriologic isolation of *B. mallei*, inoculation into guinea pigs, the mallein test or serology.

In live animals, *B. mallei* is isolated from skin lesions or blood samples. Organisms are much easier to find in fresh than in old lesions, where they may be scant. At necropsy, bacteria can also be isolated from exudates in the nasal passages and the upper respiratory tract. *B. mallei* is a nonmotile Gram negative rod; bacteria from young cultures and clinical samples are rods with bipolar staining while organisms from older cultures may be pleomorphic. On blood agar or Loeffler's serum agar, colonies are approximately 1 mm, white, semitranslucent and viscid. Older colonies turn yellow. On glycerin–potato media, a clear honey–like layer is seen by day 3; this eventually darkens to reddish–brown or brown. A polymerase chain reaction can differentiate *B. mallei* DNA from *B. pseudomallei*.

In the mallein test, a positive reaction is indicated by eyelid swelling 1 to 2 days after intrapalpebral injection of a protein fraction of *B. mallei*, or by conjunctivitis after administration in eyedrops.

A variety of serologic tests are available, including complement fixation, enzyme–linked immunosorbent assay (ELISA), indirect hemagglutination, counter–immunoelectrophoresis and immunofluorescence. The most accurate and reliable tests in horses are complement fixation and ELISA. Agglutination and precipitin tests are unreliable for horses with chronic glanders and animals in poor condition. Complement fixation tests cannot be used with donkey or mule serum.

Treatment and Vaccination

Antibiotics may be effective; however, treatment is not generally recommended, as infections can be spread to humans and other animals, and treated animals may become asymptomatic carriers. Vaccines are not available.

Morbidity and Mortality

Glanders can spread widely when large numbers of animals are in close contact; in China, 30% of horses were infected when large numbers of animals were gathered together in World War II. Acute infections are usually fatal within 1 to 2 weeks. Animals with the chronic form can sometimes survive for years.

Post–Mortem Lesions

At necropsy, there may be ulcers, nodules and stellate scars in the nasal cavity, trachea, pharynx, larynx, skin and subcutaneous tissues. Catarrhal bronchopneumonia with enlarged bronchial lymph nodes may be evident. The lungs, liver, spleen and kidneys may contain firm, rounded, encapsulated miliary gray nodules similar to tubercles. The lymphatic vessels may be swollen; the lymph nodes are typically enlarged and fibrotic and contain focal abscesses. In addition, necrosis may be noted in the internal organs and testes.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/glanders_t.htm

"Glanders and Melioidosis" in *eMedicine*
http://www.*emedicine*.com/emerg/topic884.htm

FAO Manual on meat inspection for developing countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

Foreign Animal Diseases.
United States Animal Health Association
http://www.vet.uga.edu/vpp/gray_book/FAD

Manual for the Recognition of Exotic Diseases of Livestock
http://panis.spc.int/

Material Safety Data Sheets –Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines
http://www.oie.int/eng/normes/mmanual/a_summry.htm

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook
http://www.vnh.org/BIOCASU/toc.html

References

Batts–Osborne D., P.P. Rega, A.H. Hall and T.W. McGovern. "CBRNE – Glanders and Melioidosis." *eMedicine*, Oct 2001. 17 Nov 2002 <http://www.*emedicine*.com/emerg/topic884.htm>.

Bauernfeind A., Roller C., Meyer D., Jungwirth R., and Schneider I. "Molecular procedure for rapid detection of *Burkholderia mallei* and *Burkholderia pseudomallei*." *J. Clin. Microbiol.* 36 (1998):

2737–2741.

Gilbert, R.O. "Glanders" In *Foreign Animal Diseases*. Richmond, VA: United States Animal Health Association, 1998. 14 Nov 2002 <http://www.vet.uga.edu/vpp/gray_book/FAD/gla.htm>.

"Glanders." Animal Health Australia. *The National Animal Health Information System (NAHIS)*. 4 Oct 2002 <http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha>.

"Glanders (*Burkholderia mallei*)" *Centers for Disease Control and Prevention (CDC)*, July 2002. 8 Oct 2002 < http://www.cdc.gov/ncidod/dbmd/diseaseinfo/glanders_t.htm>.

"Glanders." In Herenda, D., P.G. Chambers, A. Ettriqui, P. Seneviratna, and T.J.P. da Silva. *Manual on meat inspection for developing countries*. *FAO Animal Production and Health Paper 119*. 1994 Publishing and Multimedia Service, Information Division, FAO, 14 Nov 2002 < http://www.fao.org/docrep/003/t0756e/T0756E07.htm#ch6.2.3>.

"Glanders." In *Manual for the Recognition of Exotic Diseases of Livestock: A Reference Guide for Animal Health Staff*. Food and Agriculture Organization of the United Nations, 1998. 14 Nov 2002 <http://panis.spc.int/RefStuff/Manual/Equine/GLANDERS.HTML>.

"Glanders." In *Manual of Standards for Diagnostic Tests and Vaccines*. Paris: Office International des Epizooties, 2000. 14 Nov 2002 <http://www.oie.int/eng/normes/mmanual/A_00076.htm>.

"Glanders." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 502–3.

"Glanders and Melioidosis." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 14 Nov 2002 <http://www.vnh.org/BIOCASU/8.html>.

"Material Safety Data Sheet –*Burkholderia (Pseudomonas) mallei*." *Canadian Laboratory Centre for Disease Control*, January 2001. 14 Nov 2002 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds25e.html>.

Melioidosis

Pseudoglanders, Whitmore Disease

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY®

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Melioidosis results from infection by *Burkholderia pseudomallei*, a motile Gram negative bacillus (family Pseudomonadaceae). This organism was formerly known as *Pseudomonas pseudomallei*.

Geographic Distribution

Melioidosis is endemic in Southeast Asia, Africa, Australia, the Middle East, India and China. This infection is mainly associated with tropical and subtropical regions; however, *B. pseudomallei* has also been isolated from the temperate regions of southwest Australia and France. Isolated cases have occurred in South America and in the states of Hawaii and Georgia in the United States. *B. pseudomallei* is generally found in water or moist soil.

Transmission

New infections are primarily acquired from organisms in the environment. Contaminated swamps, muddy water and rodents are important sources of infection. Soil-borne infections are generally associated with heavy rainfall or flooding in areas with high humidity or temperatures. Infection can occur by ingestion, inhalation, or through wounds and abrasions. The role of insect bites is uncertain. Direct human-to-human and animal-to-human transmission is rare but can occur after contact with blood or body fluids. Depending on the site of the infection, contaminated body fluids may include urine, nasal secretions and milk. Shed organisms can survive for months in soil and water.

Disinfection

B. pseudomallei can survive for months to years in soil and water, but can be readily destroyed by heat. Moist heat of 121°C for at least 15 min or dry heat of 160-170°C for at least 1 hour is recommended for disinfection. The organism is also susceptible to numerous disinfectants, including 1% sodium hypochlorite, 70% ethanol, glutaraldehyde and formaldehyde.

Infections in Humans

Incubation Period

In natural infections, the incubation period can vary from two days to months or years. Infections may remain latent for years. Infections from aerosolized forms in biological weapons are expected to have an incubation period of 10-14 days.

Clinical Signs

B. pseudomallei infections may be inapparent or can result in pulmonary infections, disseminated septicemia, acute nondisseminated septicemia or localized chronic suppurative infections.

The most serious form is disseminated septicemic infection. In natural infections, this form is most common in people with pre-existing debilitating diseases such as AIDS, cancer, diabetes and kidney failure. Its onset may be acute. The clinical signs may include severe headache, severe dyspnea, disorientation, pharyngitis, upper abdominal pain, diarrhea, pustular skin lesions and notable muscle tenderness. Pulmonary signs and symptoms of arthritis or meningitis are sometimes seen. This form is often accompanied by septic shock.

Pulmonary infections vary in severity, from mild bronchitis to severe necrotizing pneumonia. Symptoms can appear suddenly or gradually and may include fever, headache, cough, tachypnea, rales, blood-tinged sputum, anorexia, generalized myalgia and dull aching or pleuritic chest pain.

Localized chronic suppurative infections are characterized by abscesses in the skin, lymph nodes or other organs including the brain. Osteomyelitis is common with this form. Fever may or may not be present. Acute nondisseminated septicemic infection also occurs, involves a single organ and is relatively rare.

In cases with acute infection of the oral, nasal or conjunctival mucosa, the clinical signs may include mucopurulent, blood streaked nasal discharge from the nose, as well as nodules and ulcerations in the septum and turbinates.

Communicability

Yes. Direct transmission between humans or from humans to animals is rare but can occur after contact with blood or body fluids. Depending on the site of the infection, contaminated body fluids may include urine, nasal secretions and milk. Human carriers have not been seen.

Diagnostic Tests

Melioidosis can be diagnosed by isolation and identification of *Burkholderia pseudomallei*. Bacteria may be found in blood, sputum, tissues and wound exudates. In the septicemic form, blood cultures may be negative until just before death.

The organism has a wrinkled colony form, which may be mixed with smooth colonies. A characteristic odor has been described. (Due to the risk of infection, directly sniffing the plates is not recommended.) Organisms are oval, Gram negative bacilli, with bipolar staining in young cultures. A polymerase chain reaction can differentiate *B. mallei* DNA from *B. pseudomallei*.

Serologic tests on paired sera may be helpful. High single titers in the presence of clinical signs may also be used for diagnosis. Serologic tests include agglutination tests, indirect hemagglutination, complement fixation, immunofluorescence assays and enzyme immunoassays. Cross-reactions may occur in serologic tests with *Burkholderia mallei*, the causative agent of glanders.

Treatment and Vaccination

B. pseudomallei is variably susceptible to antibiotics. Long-term treatment may be necessary and multiple drugs may be needed. Pulmonary resection or draining of abscesses is sometimes necessary for chronic cases. No vaccine is available.

Morbidity and Mortality

In natural infections, the mortality rate is usually less than 10%, except in disseminated septicemic infections; mortality rates as high as 90% may be seen in this form. Localized lesions may be progressive or disseminate. Fatal infections are more common in patients who are immunosuppressed or have concurrent disease.

Exposure to biological weapons containing aerosolized forms is expected to result in septicemia or severe pulmonary infections, with high mortality rates in spite of treatment.

Infections in Animals

Species Affected

Infection with *B. pseudomallei* is seen most often in pigs, goats and sheep. It occurs less often in cattle, horses, dogs, rodents, birds, dolphins, tropical fish, primates and various wild animals. Hamsters, guinea pigs and rabbits can be infected in the laboratory.

Incubation Period

The incubation period can vary from days to months or years. Abscesses may be carried without symptoms.

Clinical Signs

B. pseudomallei infection results in suppurating or caseous lesions in lymph nodes or other organs. Infections may be asymptomatic and abscesses may be found in clinically normal goats, sheep and pigs. Symptomatic melioidosis mimics other diseases; the clinical signs vary with the site of the lesion. They may include fever, loss of appetite, and lymphadenopathy, often involving the submandibular nodes in pigs. Lameness or posterior paresis, nasal discharge, encephalitis, gastrointestinal symptoms or respiratory signs may also be seen in some species. Extensive abscesses and infections of vital organs can be fatal.

In sheep and goats, lung abscesses and pneumonia are common. Other common symptoms in sheep include high fever, coughing, ocular and nasal discharge, lameness with swollen joints, neurologic disease, and gradual emaciation. Some animals may display only weakness and fever. Mastitis is sometimes seen in goats and the superficial lymph nodes and udder may contain palpable abscesses. Pulmonary lesions in goats are usually less severe than in sheep and coughing is not prominent. In horses, neurologic disease, respiratory symptoms, or colic and diarrhea have been described. Infections in pigs are usually chronic and asymptomatic. Acute infections in this species may result in septicemia with fever, anorexia, coughing and nasal and ocular discharges. Abortions and stillbirths may occur but are rare, and orchitis may occur in boars. Cattle are rarely affected, but may develop pneumonia or neurologic signs.

Communicability

Yes. Direct transmission between animals or from animals to humans is rare but can occur after contact with blood or body fluids. Depending on the site of the infection, contaminated body fluids may include urine, nasal secretions and milk. Animals may become carriers.

Diagnostic Tests

Swabs of nasal discharges and samples collected from lesions should be submitted for culture. Organisms may be isolated from the sputum, blood, wound exudates

or tissues. In some species, serum may also be collected for serologic tests.

Melioidosis is diagnosed by isolation and identification of *Burkholderia pseudomallei*. This organism has a wrinkled colony form, which may be mixed with smooth colonies. A characteristic odor has been described. (Due to the risk of infection, directly sniffing the plates is not recommended.) Organisms are oval, Gram negative bacilli, with bipolar staining in young cultures. A polymerase chain reaction can differentiate *B. mallei* DNA from *B. pseudomallei*.

In some species, agglutination tests, indirect hemagglutination, immunofluorescence, and enzyme immunoassays can be used for diagnosis. Cross-reactions may occur in serologic tests with *Burkholderia mallei*, the causative agent of glanders.

Treatment and Vaccination

B. pseudomallei is susceptible to various antibiotics, but relapses can occur when treatment is stopped. Vaccines are available in some countries but are not effective against large challenge doses.

Morbidity and Mortality

Mortality varies with the site of the lesions, but can be high in sheep. Extensive abscesses and infections of vital organs can be fatal. Disseminated septicemic infections have a high mortality rate, but are less common in animals than humans. Infections may be progressive.

Post-Mortem Lesions

At necropsy, the major findings are multiple abscesses containing thick, caseous greenish-yellow or off-white material. These abscesses are generally not calcified. The regional lymph nodes, spleen, lung, liver and subcutaneous tissues are most often involved, but abscesses can occur in most organs. In acute cases, pneumonic changes in the lungs, meningoencephalitis and suppurative polyarthritis may be found. In cases with suppurative arthritis, the joints may contain fluid and large masses of greenish-yellow purulent material.

In sheep, common findings include abscesses and suppuration in the nasal mucosa. Splenic abscesses are often found in pigs at slaughter.

Internet Resources

Material Safety Data Sheets–
Canadian Laboratory Center for Disease Control
http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/index.html#menu

Manual for the Recognition of Exotic Diseases of Livestock

http://panis.spc.int/

Centers for Disease Control and Prevention (CDC)

http://www.cdc.gov/ncidod/dbmd/diseaseinfo/melioidosis_g.htm

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

Animal Health Australia.
The National Animal Health Information System (NAHIS)

http://www.brs.gov.au/usr-bin/aphb/ahsq?dislist=alpha

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

References

Bauernfeind A., Roller C., Meyer D., Jungwirth R., and Schneider I. "Molecular procedure for rapid detection of Burkholderia mallei and Burkholderia pseudomallei." *J. Clin. Microbiol*. 36 (1998): 2737-2741.

Bogle, R.B. "Bioterrorism: Hype or Hazard?" Cactus Chronicle (*Arizona Society for Clinical Laboratory Science*) 23, no. 1 (January/February 2000): 7 Oct 2002 <http://pw1.netcom.com/~aguldo/agga/txt/cactusbt.htm>.

Gilbert, R.O. "Glanders" In *Foreign Animal Diseases*. Richmond, VA: United States Animal Health Association, 1998. 7 Oct 2002 <http://www.vet.uga.edu/vpp/gray_book/FAD/gla.htm>.

"Glanders and Melioidosis." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 26 Oct 2002 <http://www.usdpi.org/glanders_and_m__-_dod_medical_guide.htm>.

Herenda, D., P.G. Chambers, A. Ettriqui, P. Seneviratna, and T.J.P. da Silva. "*Manual on meat inspection for developing countries*. *FAO Animal Production and Health Paper 119*." 1994 Publishing and Multimedia Service, Information Division, FAO, 8 Oct 2002 <http://www.fao.org/docrep/003/t0756e/t0756e00.htm>.

Jesudason M.V., W.S. Anandaraj and B. Malathi. "An indirect ELISA for the diagnosis of melioidosis." *J. Med. Res.* 114 (Aug 2001):51-3.

"Material Safety Data Sheet –*Burkholderia* (*Pseudomonas*) *pseudomallei*." January 2001 *Canadian Laboratory Centre for Disease Control*. 4 October 2002 <http://www.hc-sc.gc.ca/pphb-

dgspsp/msds-ftss/msds26e.html>.

"Melioidosis." Animal Health Australia. *The National Animal Health Information System (NAHIS)*. 4 Oct 2002 <http://www.brs.gov.au/usr-bin/aphb/ahsq?dislist=alpha>.

"Melioidosis." In *Manual for the Recognition of Exotic Diseases of Livestock: A Reference Guide for Animal Health Staff*. Food and Agriculture Organization of the United Nations, 1998. 8 Oct 2002 < http://panis.spc.int/RefStuff/Manual/Multiple%20Species/MELIOIDOSIS.HTML>.

"Melioidosis." In *The Merck Manual*, 17th ed. Edited by M.H. Beers and R. Berkow. Whitehouse Station, NJ: Merck and Co., 1999. 7 Oct 2002 <http://www.merck.com/pubs/mmanual/section13/chapter157/157d.htm>.

"Melioidosis." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 481-2.

"Melioidosis (*Burkholderia pseudomallei*)" *Centers for Disease Control and Prevention (CDC)*. 8 Oct 2002 <http://www.cdc.gov/ncidod/dbmd/diseaseinfo/melioidosis_g.htm>.

Vadivelu, J. and S.D. Puthucheary. "Diagnostic and prognostic value of an immunofluorescent assay for melioidosis." *The American Journal of Tropical Medicine & Hygiene* 62, no. 2 (2000): 297–300.

Plague

Peste, Black Death, Bubonic Plague, Pneumonic Plague, Septicemic Plague, Pestis Minor

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Plague results from infection by *Yersinia pestis*, a non–motile, facultatively intracellular, Gram negative rod (family Enterobacteriaceae).

Geographic Distribution

Plague is seen in parts of North and South America, Africa, the Middle East, Central and Southeast Asia and Indonesia. Foci of infection are found in the former Soviet Union. This disease does not occur in Europe, Australia or Japan.

Transmission

Plague is usually spread between rodents or humans by the bites of infected fleas. Vectors include a variety of rodent fleas, particularly the oriental rat flea (*Xenopsylla cheopis*). In the U.S., the most common vector is *Oropsylla montana*, a flea often found on California ground squirrels, rock squirrels, and sometimes other rodents including prairie dogs. Human fleas (*Pulex irritans*) may also carry *Y. pestis*. *Y. pestis* is also present in the tissues and body fluids of infected animals; these bacteria can be transmitted directly through mucous membranes and broken skin. Aerosols from people or animals with the pneumonic form are infectious and animals may transmit bacteria in bites. Carnivores often become infected when they eat diseased rodents.

In the wild, *Y. pestis* is maintained in cycles between wild rodents and fleas; sporadic cases occur in humans and domestic animals when they come into contact with infected animals or fleas. Infection of rodents in urban areas, particularly the Roof rat or Norway rat, can result in epizootic and epidemic plague in humans. Direct person–to–person transmission can occur in pneumonic plague.

Y. pestis can survive for long periods of time in organic material; it may remain viable for up to 100 days in blood and for as long as 9 months in human bodies. Infectious bacteria can also be found in water, moist soil and grains for several weeks. *Y. pestis* is not resistant to desiccation or heat: it is destroyed by exposure to 55°C for 15 minutes or several hours in sunlight.

Disinfection

Y. pestis is susceptible to a number of disinfectants including 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, formaldehyde and iodine–based and phenolic disinfectants. It can also be inactivated by moist heat (121° C for at least 15 min) or dry heat (160–170° C for at least 1 hour).

Infections in Humans

Incubation Period

The incubation period for pneumonic plague is 1 to 3 days. The symptoms of bubonic plague appear after 2 to 6 days.

Clinical Signs

Three major forms of plague are seen in humans: bubonic plague, septicemic plague, pneumonic plague.

Bubonic plague appears acutely; the initial symptoms may include fever, headache, malaise and myalgia. Vomiting, nausea, abdominal pain, hepatomegaly and splenomegaly are sometimes seen. Patients with bubonic plague typically develop an infected, swollen, and very painful draining lymph node, called a bubo; the bubo is often one of the femoral or inguinal lymph nodes. Other lymph nodes, or multiple nodes, may also be involved. In some cases, a pustule, vesicle, eschar or papule occurs at the site of the flea bite.

Bubonic plague can develop into septicemic plague. Bacteremia is present in most cases of bubonic plague but the symptoms of septicemia – including high fever, chills, malaise, nausea, vomiting, abdominal pain, diarrhea and hypotension – do not always develop. Meningitis is relatively rare; it occurs in approximately 6% of people with the septicemic or pneumonic forms. Thrombo*s*es in blood vessels can cause necrosis and

gangrene of the extremities or disseminated intravascular coagulation (DIC).

Pneumonic plague occurs after inhalation of bacteria or after blood–borne spread to the lungs. Pneumonic plague is expected to be the predominant form in a bioterrorist attack. The symptoms of pneumonic plague develop acutely and include high fever, chills, headache, myalgia and malaise. Nausea, vomiting, diarrhea and abdominal pain may be seen. Within 24 hours, a cough with bloody sputum develops; the sputum contains only specks of blood at first but eventually becomes foamy and pink or red. Cervical buboes occur rarely. Pneumonic plague is rapidly fatal, with dyspnea, stridor and cyanosis ending in respiratory failure and circulatory collapse.

Pestis minor is a benign form of bubonic plague, usually seen only in regions where plague is endemic. Pestis minor is characterized by fever, lymphadenitis, headache and prostration. These symptoms resolve spontaneously within a week.

Communicability

In the United States, person–to–person transmission of bubonic plague has not occurred since 1924; however, person–to–person transmission is seen in epidemics in some countries. Pneumonic plague can be highly contagious, particularly under crowded conditions

Diagnostic Tests

A presumptive diagnosis can be made by identifying the characteristic organisms in sputum, blood, lymph node (bubo) aspirates or cerebrospinal fluid; *Y. pestis* is a Gram negative, non–motile, facultative intracellular coccobacillus with bipolar staining. Organisms can be identified by immunofluorescence. Immunoassays can also detect *Y. pestis* antigens in serum. Polymerase chain reaction (PCR) assays are used in research. Bacteriophage typing can be helpful in tracing outbreaks.

Plague can also be diagnosed by isolation of *Y. pestis*. Organisms can be recovered from sputum, blood or aspirates of lymph nodes and may be cultured on ordinary media including blood agar, MacConkey agar or infusion broth. Automated systems may misidentify this bacterium, as it grows slowly and biochemical reactions may be delayed. Guinea pig inoculation can also be used.

Serology is occasionally helpful. A fourfold rise in titer is diagnostic. Latex agglutination is most often used, but passive hemagglutination tests and complement fixation are also available.

Treatment and Vaccination

Antibiotics are effective in the early stages of bubonic or pneumonic plague; in pneumonic plague, their efficacy is often limited after 24 hours. Buboes are occasionally drained but usually resolve with antibiotic treatment.

Vaccines may be available for people with occupational risk factors; these vaccines are not wholly protective, particularly against the pneumonic form. A whole cell vaccine was marketed until November 1998 but appears to have been taken off the market. A new vaccine is in development and may be more effective against both forms of plague.

Morbidity and Mortality

The mortality rate is approximately 50 to 60% for untreated bubonic plague and nearly 100% for untreated pneumonic plague. The pneumonic form is often fatal within 48 hours after it becomes symptomatic. Early treatment reduces the mortality rate to less than 5%; however, treatment for the pneumonic form must be started during the first 24 hours after symptoms begin.

Worldwide, approximately 1,000 to 2,000 cases of plague are seen annually; epidemics occur regularly in Africa and Asia. Sporadic cases also occur in North and South America after exposure to wild rodents and fleas. In the United States, approximately 18 cases of plague were seen yearly during the 1980s; the mortality rate for these cases was approximately 14%.

Infections in Animals

Species Affected

More than 200 species of mammals can be infected with *Y. pestis*. Rodents are the reservoir hosts. Many rodents, including prairie dogs, chipmunks, wood rats, ground squirrels, deer mice and voles suffer occasional epidemics or maintain the virus in natural cycles. Rock squirrels and the California ground squirrel are often the sources of human infections in the United States. Rats are usually the carriers for epidemics in humans. Rabbits, wild carnivores, domestic cats and dogs can develop plague when they are exposed to infected rodents or their fleas; among carnivores, cats are particularly susceptible.

Incubation Period

Clinical signs develop can develop within 3–4 days in experimentally infected cats.

Clinical Signs

Asymptomatic infections and mild illness are typical in some reservoir hosts. Wild carnivores including coyotes, skunks and raccoons can also seroconvert without clinical disease. Other animals may have fever, lymphadenitis, abscesses in internal organs, or sudden death from sepsis.

In cats, clinical signs can include fever, anorexia, dehydration and depression. Infected cats may develop enlarged lymph nodes near the site of infection: the submandibular or cervical lymph nodes are most often involved. Infected lymph nodes can develop abscesses, ulcerate and drain. Swellings may also be seen around the

head, neck and eyes. Sneezing, hemoptysis, incoordination, quadriplegia, necrotic tonsillitis and symptoms of pneumonia may occur.

Dogs seem to be relatively resistant to plague and animals may seroconvert without symptoms. High fevers and lymphadenopathy, with occasional deaths, have also been seen. Ten experimentally infected dogs developed a fever and other signs of illness but recovered spontaneously during the next week.

Communicability

Yes. Bacteria can be transmitted in aerosols, by direct contact with tissues and body fluids, and in bites. Infected fleas can transmit bacteria for months.

Diagnostic Tests

Plague can be diagnosed by isolation of *Y. pestis*; bacteria may be found in blood, nasal swabs, lymph node aspirates, transtracheal aspirates and tissue samples. If neurologic signs are present, cerebrospinal fluid (CSF) may yield bacteria. *Y. pestis* is a Gram negative, non–motile, facultative intracellular coccobacillus with bipolar staining. The organism can be identified by immunofluorescence or antigen–capture enzyme linked immunosorbent assays (ELISAs).

Organisms can also be cultured; *Y. pestis* will grow on ordinary media including blood agar, MacConkey agar or infusion broth. Automated systems may misidentify this bacterium, as it grows slowly and biochemical reactions may be delayed. Guinea pig inoculation can also be used. A rise in titer in paired serum samples is diagnostic, if the animal survives; the latex hemagglutination and passive hemagglutination tests (PHA) are often used.

Treatment and Vaccination

Early treatment with antibiotics can be successful.

Morbidity and Mortality

In endemic areas, many rodents – including chipmunks, wood rats, ground squirrels, deer mice and voles – suffer occasional epidemics. Mortality in some rodent species can be high; infections are fatal in nearly 100% of prairie dogs. Between outbreaks, bacteria seem to cycle in reservoir populations without causing high mortality

The mortality rate is 50% in cats fed plague–infected mice; sick cats may die within 1 to 2 days or after several weeks. Dogs, coyotes, raccoons, skunks and other carnivores often seroconvert without symptoms; clinical infections and deaths are relatively rare in these species. Ten experimentally infected dogs recovered spontaneously.

Post–Mortem Lesions

Post mortem lesions vary with the type of infection. Signs can include lymphadenopathy, bacterial pneumonia with lung hemorrhages, and necrosis in the liver, spleen and other internal organs.

Internet Resources

Centers for Disease Control and Prevention (CDC) Plague Pages

http://www.bt.cdc.gov/agent/plague/index.asp

Material Safety Data Sheets–Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

References

Biberstein, E.L. and J. Holzworth. "Bacterial Diseases. Plague." In *Diseases of the Cat.* Edited by J. Holzworth. Philadelphia, PA: W.B. Saunders, 1987, p. 294; 660.

Collins, F.M. "Pasteurella, Yersinia, and Francisella." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 20 November 2002 <http://www.gsbs.utmb.edu/microbook/ch029.htm>.

"Bacterial infections caused by Gram–negative bacilli. Enterobacteriaceae." In *The Merck Manual*, 17th ed. Edited by M.H. Beers and R. Berkow. Whitehouse Station, NJ: Merck and Co., 1999. 8 Nov 2002 <http://www.merck.com/pubs/mmanual/section13/chapter157/157d.htm>.

Butler, T. In *Zoonoses*. Edited by S.R. Palmer, E.J.L. Soulsby and D.I.H Simpson. New York: Oxford University Press, 1998, pp. 286–292.

"Control of Communicable Diseases." Edited by J. Chin. American Public Health Association, 2000, pp.532–535.

"Information on plague." *Centers for Disease Control and Prevention (CDC)*, June 2001. 19 Nov 2002 < http://www.cdc.gov/ncidod/dvbid/plague/info.htm>.

Macy, D.W. "Plague." In *Infectious Diseases of the Dog and Cat*. Edited by C.E. Greene. Philadelphia: W.B. Saunders, 1998, pp. 295–300.

Macy, D.W. "Plague." In *Current Veterinary Therapy X. Small Animal Practice*. Edited by R.W. Kirk and J.D. Bonagura. Philadelphia: W.B. Saunders, 1989, pp. 1088–91.

"Material Safety Data Sheet –*Yersinia pestis*." *Canadian Laboratory Centre for Disease Control*, March 2001. 20 November 2002 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds169e.html>.

"Plague." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 19 Nov 2002 <http://www.vnh.org/BIOCASU/9.html>.

"Plague." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 485–6.

Psittacosis

Avian Chlamydiosis, Ornithosis, Parrot Fever

Last Updated: Jan. 2004

Etiology

In birds, avian chlamydiosis results from infection by *Chlamydophila psittaci* (order Chlamydiales, family Chlamydiaceae). Psittacosis is the human disease caused by infection with *Chlamydophila psittaci*. This organism, previously known as *Chlamydia psittaci*, is a Gram negative, coccoid, obligate intracellular bacterium. There are at least six avian serotypes.

Geographic Distribution

Avian chlamydiosis can be found worldwide. *C. psittaci* is particularly common in psittacine birds in tropical and subtropical regions. This disease is present in the United States. In a 1982 survey, *C. psittaci* was isolated from 20–50% of necropsied pet birds in California and Florida.

Transmission

Among birds, *C. psittaci* is transmitted frequently by inhalation of infectious dust and occasionally by ingestion. Fomites can also spread chlamydiosis, and biting insects, mites, and lice may be important in mechanical transmission. Birds can be asymptomatic carriers; carriers shed *C. psittaci* intermittently, particularly when stressed. One form of the organism, the elementary body, can survive in dried feces for months.

Humans usually become infected after inhaling contaminated dust from feathers or bird droppings. Direct contact with infected birds and bites can also spread the disease. Person–to–person transmission is rare but can occur by aerosol or venereal spread.

Disinfection

C. psittaci is susceptible to quaternary ammonium compounds, chlorophenols, iodophore disinfectants, formaldehyde, 80% isopropyl alcohol or a 1:100 dilution of household bleach.

Infections in Humans

Incubation Period

The incubation period in humans is 1 to 4 weeks; most infections become symptomatic after 10 days.

Clinical Signs

Psittacosis can be acute or insidious in onset. The disease varies from a mild, flu–like infection with a fever, chills, headaches, anorexia, malaise, sore throat and photophobia to a serious atypical pneumonia with dyspnea. There may be a dry cough, which sometimes becomes mucopurulent. In uncomplicated infections, the fever lasts for approximately 2 to 3 weeks then resolves. More rarely, a severe systemic illness with endocarditis, myocarditis and renal complications can develop. Hepatitis and neurologic complications including encephalitis, meningitis and myelitis have also been seen.

Communicability

Person–to–person transmission is rare; the agent is occasionally spread in aerosols during paroxysmal coughing. Venereal transmission has also been reported.

Diagnostic Tests

Psittacosis can be diagnosed by isolation of *C. psittaci* or by serology. *C. psittaci* can be isolated in embryonated eggs, laboratory animals, or cell cultures of buffalo green monkey (BGM), African green monkey (Vero), McCoy or L cells. Iodine staining of inclusion bodies or immunofluorescence can differentiate *C. psittaci* from *C. trachomatis*. DNA restriction endonuclease analysis can also distinguish these two organisms in tissue samples. Serologic tests include complement fixation or immunofluorescent tests; individuals treated with antibiotics may not develop antibodies. A presumptive diagnosis is sometimes made, based on exposure to birds and clinical signs.

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Treatment and Vaccination

Antibiotics (tetracycline) combined with supportive care are effective. There is no vaccine.

Morbidity and Mortality

Currently, fewer than 50 confirmed cases are reported annually in the United States; additional undiagnosed or unreported cases are thought to occur. The disease may be mild or severe, depending on age and health of the individual and the extent of pneumonia; more serious disease is usually seen in the elderly and those who are debilitated. The mortality rate can be as high as 30% in severe infections left untreated; treated cases are rarely fatal. Convalescence may be slow after severe disease.

Infections in Animals

Species Affected

Avian chlamydiosis occurs in most birds, but is particularly common in psittacine birds, pigeons, doves, and mynah birds. This disease is sometimes seen in ducks and turkeys but only rarely in chickens.

Incubation Period

The incubation period in cage birds is usually three days to several weeks. However, in latent infections, active disease may be seen years after infection.

Clinical Signs

In turkeys, ducks, and pigeons, the clinical signs can include depression, ruffled feathers, weakness, inappetence, weight loss, nasal discharge, respiratory distress, yellowish–green or green diarrhea, and unilateral or bilateral conjunctivitis. Egg production is decreased. Nervous signs may be seen, including transient ataxia in pigeons and trembling or gait abnormalities in ducks.

In pet birds, common symptoms include anorexia, weight loss, diarrhea, yellowish droppings, sinusitis, respiratory distress, nervous signs, and conjunctivitis. Asymptomatic infections and mild infections with diarrhea or mild respiratory signs may also be seen. Residual disturbances in feathering may be apparent in survivors.

Communicability

Infected birds can shed *C. psittaci* for weeks to months. Shedding may be continuous or intermittent.

Diagnostic Tests

In live birds, avian chlamydiosis is usually diagnosed by isolating *C. psittaci* from pharyngeal or nasal swabs, feces, cloacal swabs, conjunctival scrapings or peritoneal exudate. At necropsy, the organism may be isolated from blood, ocular or nasal exudates, inflammatory exudates, or tissue samples from the lung, kidney, spleen, liver, and pericardium. If diarrhea is present, organisms may be found in the colonic contents or feces.

C. psittaci is isolated in embryonated eggs, laboratory animals or cell cultures of buffalo green monkey (BGM), African green monkey (Vero), McCoy or L cells. The organisms can be identified by direct immunofluorescence or other staining techniques. A single negative culture may be misleading, as carrier birds may shed *C. psittaci* only intermittently. Treatment with antibiotics during the 2 to 3 weeks before testing may also lead to false negatives.

Avian chlamydiosis can also be diagnosed by demonstrating *C. psittaci* in tissues, feces, or exudates by histochemical or immunohistochemical staining. Antigen capture enzyme–linked immunosorbent assays (ELISAs) are also used, but may lack sensitivity or cross–react with other Gram negative bacteria. Polymerase chain reaction (PCR) and polymerase chain reaction/ restriction fragment length polymorphism (PCR–RFLP) assays have been described.

Serology is occasionally helpful. At least a four–fold rise in titer should be seen in paired samples. Complement fixation is the standard test. Other assays include ELISA, latex agglutination (LA), elementary body agglutination (EBA), micro–immunofluorescence (MIFT), and agar gel immunodiffusion tests. The EBA test detects IgM only and can be used to diagnose current infections.

Treatment and Vaccination

Antibiotics are effective in treating the symptoms of avian chlamydiosis, but some birds may remain infected.

Morbidity and Mortality

Morbidity and mortality vary with the host species and pathogenicity of the serotype. Young birds tend to be more susceptible than older birds. In turkeys, serovar D strains cause 50–80% morbidity and 10–30% mortality. In broiler turkeys, up to 80% of infections with this serovar may be fatal. Other serovars in turkeys usually result in 5–20% morbidity, with mortality under 50%. In ducks, morbidity may be up to 80% and mortality 0–40%. Concurrent infections or stress increase the severity of the disease.

Post–Mortem Lesions

Post–mortem lesions in birds can include pneumonia, airsacculitis, hepatitis, myocarditis, epicarditis, nephritis, peritonitis, and splenitis. In turkeys, an enlarged and congested spleen may be the only lesion. Wasting, vascular congestion, fibrinous airsacculitis, fibrinous pericarditis, fibrinous pneumonia with congestion of the lungs, or fibrinous perihepatitis may also be seen. In pigeons, common lesions include hepatomegaly, airsacculitis, enteritis, and conjunctivitis with swollen and encrusted eyelids. The spleen may rupture. In cage

birds, the liver may be enlarged and yellow with focal necrosis. The spleen is often enlarged, with white foci. Airsacculitis, pericarditis, and congestion of the intestinal tract can also be seen.

Internet Resources

Centers for Disease Control and Prevention (CDC)

http://www.cdc.gov/ncidod/dbmd/diseaseinfo/psittacosis_t.htm

Material Safety Data Sheets–
Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines

http://www.oie.int/eng/normes/mmanual/a_summry.htm

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

References

"Avian Chlamydiosis." In *Whiteman and Bickford's Avian Disease Manual,* 4th ed. Edited by B.R. Charlton et al. Kennett Square, Pa: American Association of Avian Pathologists, 1996, pp. 68–71.

"Avian Chlamydiosis." In *Manual of Standards for Diagnostic Tests and Vaccines*. Paris: Office International des Epizooties, 2000, pp. 679–90.

Becker, Y. "Chlamydia." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 14 Nov 2002 <http://www.gsbs.utmb.edu/microbook/ch039.htm>.

"Chlamydiosis." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 1300–01.

"Chlamydiosis." In *Poultry Diseases*, 4th ed. Edited by F.T.W. Jordan and M. Pattison. London: W.B. Saunders, 1996, pp. 94–99.

Gerlach, H. "Chlamydia." In *Clinical Avian Medicine and Surgery*. Edited by G.J. Harrison and L. Harrison. Philadelphia: W.B. Saunders, 1986, pp. 457–63.

Johnston W.B., M. Eidson, K.A. Smith, and M.G. Stobierski. "Compendium of chlamydiosis (psittacosis) control, 1999." Psittacosis Compendium Committee, National Association of State Public Health Veterinarians. *Journal of the American Veterinary Medical Association* 214, no. 5 (1999): 640–6.

"Material Safety Data Sheet –*Chlamydia psittaci*." January 2001 *Canadian Laboratory Centre for Disease Control*. 1 November 2001 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds31e.html>.

National Association of State Public Health Veterinarians. Compendium of Measures To Control Chlamydophila psittaci (formerly Chlamydia psittaci) Infection Among Humans (Psittacosis) and Pet Birds, 2004. AVMA Online. <http://www.avma.org>.

"Psittacosis." *Centers for Disease Control and Prevention (CDC)*, July 2002. 14 Nov 2002 <http://www.cdc.gov/ncidod/dbmd/diseaseinfo/psittacosis_t.htm>.

"Psittacosis." In *The Merck Manual*, 17th ed. Edited by M.H. Beers and R. Berkow. Whitehouse Station, NJ: Merck and Co., 1999. 14 Nov 2002 <http://www.merck.com/pubs/mmanual/section6/chapter73/73j.htm>.

Vanrompay D., R. Ducatelle, and F. Haesebrouck. "Chlamydia psittaci infections: a review with emphasis on avian chlamydiosis." *Veterinary Microbiology* 45, no. 2–3 (1995): 93–119.

Q Fever

Query Fever

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Q fever results from infection by *Coxiella burnetii*. This organism is an obligate intracellular pathogen and has been traditionally placed in the family Rickettsiaceae; however, recent phylogenetic studies have demonstrated that *C. burnetii* is more closely related to Legionella, Francisella and Rickettsiella in the gamma subdivision of Proteobacteria.

C. burnetii forms unusual spore–like structures that are highly resistant to environmental conditions. The organism also has two distinct antigenic phases. Phase I is pathogenic and is found in infected animals or in nature; phase II is less pathogenic and is recovered after bacteria are passaged repeatedly in cell cultures or eggs.

Geographic Distribution

Q fever has been found worldwide, except in New Zealand.

Transmission

C. burnetii can be transmitted by aerosols or direct contact; it is also spread by ingestion of an infected placenta, other reproductive discharges or milk. Organisms localize in the mammary glands, supramammary lymph nodes, uterus and placenta in domestic ruminants and other susceptible species; bacteria can be shed in milk, the placenta and reproductive discharges during subsequent pregnancies and lactations. *C. burnetii* can also be found in the feces and urine. Ticks seem to spread infections among ruminants and sometimes people. Transmission has occurred in blood transfusions and by sexual contact in humans. Organisms have also been found in the semen of bulls. Vertical transmission is possible but rare.

C. burnetii is highly resistant to environmental conditions and is easily spread by aerosols; infectious airborne particles can travel a half–mile or more. Viable organisms can be found for up to 30 days in dried sputum, 120 days in dust, 49 days in dried urine from infected guinea pigs, and for at least 19 months in tick feces. At 4–6°C, organisms can survive for 42 months in milk and 12 to 16 months in wool.

Disinfection

C. burnetii is highly resistant to physical and chemical agents. Variable susceptibility has been reported for hypochlorite, formalin and phenolic disinfectants; a 0.05% hypochlorite, 5% peroxide or 1:100 solution of Lysol® may be effective. *C. burnetii* is also susceptible to glutaraldehyde, ethanol, gaseous formaldehyde, gamma irradiation or temperatures of 130°C for 60 min. High temperature pasteurization destroys the organism.

Infections in Humans

Incubation Period

In humans, the incubation period varies from 2 to 40 days; the typical incubation period is approximately 2 to 5 weeks.

Clinical Signs

The symptoms of Q fever appear acutely and can include fever, chills, a severe headache, fatigue, malaise, myalgia and chest pains. The illness generally lasts from a week to more than 3 weeks. A nonproductive cough, with pneumonitis on X–ray, sometimes develops during the second week. In severe cases, lobar consolidation and pneumonia may occur; severe infections are particularly common in elderly or debilitated patients. Hepatitis is seen in approximately one third of patients with prolonged disease; the clinical signs may include fever, malaise, right upper abdominal pain, hepatomegaly and sometimes jaundice. In pregnant women, infections can result in premature delivery, abortion and placentitis.

Complications are not common but may include chronic hepatitis, aseptic meningitis, encephalitis, osteomyelitis, vasculitis and endocarditis. Endocarditis usually

occurs in people who have pre–existing damage to the heart valves. The symptoms are similar to subacute bacterial endocarditis.

Communicability

Person to person spread is very rare but has been seen in people with pneumonia.

Diagnostic Tests

In humans, Q fever is usually diagnosed by serology. Serologic tests can be done as early as the second week of illness; they may include immunofluorescence, ELISA, agglutination or complement fixation. Antibodies to the protein antigens found in phase II organisms appear in acute Q fever; antibodies to the lipopolysaccharide of phase I organisms indicate chronic Q fever. Organisms are occasionally found in stained tissue samples but this test is not routinely used in humans.

Isolation of *C. burnetii* is dangerous to laboratory personnel and is rarely done. Organisms can be recovered from blood samples; bacteria are isolated in cell cultures, embryonated chicken eggs or laboratory animals including mice, hamsters and guinea pigs. Blood cultures from patients with endocarditis are usually negative.

Treatment and Vaccination

Antibiotics can shorten the course of acute illness and reduce the risk of complications. Treatment of chronic cases is more difficult and may require long–term antibiotic therapy. Surgical replacement is sometimes necessary for damaged valves.

Effective vaccines may be available for people who are occupationally exposed. A licensed vaccine is available in Australia. In the United States, an investigational vaccine can be obtained from special laboratories such as the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID).

Morbidity and Mortality

Most cases of Q fever occur in people occupationally exposed to farm animals or their products: farmers, abattoir workers, researchers, laboratory personnel, dairy workers and woolsorters have an increased risk of infection. Approximately 60% of cases are thought to be asymptomatic. An additional 38% of infected people experience mild illness, while 2% develop severe disease and require hospitalization.

Q fever is usually a self–limiting illness; most cases resolve spontaneously within 2 days to 2 weeks. The mortality rate is 1% in untreated cases and lower in those who are treated. A biological attack with aerosolized organisms is expected to be similar to a natural outbreak.

Infections in Animals

Species Affected

Sheep, goats and cattle are the most common domestic animal reservoirs. Dogs, cats, rabbits, horses, pigs, camels, buffalo, rodents, pigeons, geese and other fowl may carry *C. burnetii*. Antibodies to *C. burnetii* have been found in badgers, coyotes, raccoons, opossums, badgers, jackrabbits, feral pigs, black bears and musk ox. Ticks and wild birds can also harbor this organism.

Incubation Period

The incubation period is variable; reproductive failure is usually the only symptom in animals. Abortions generally occur late in pregnancy.

Clinical Signs

Abortion, stillbirth, retained placenta, endometritis, infertility and small or weak offspring can be seen in ruminants, cats, dogs, rabbits and other species. Most abortions occur near term. Several abortions may be followed by uncomplicated recovery, particularly in small ruminants; in other cases, the disease may recur yearly.

With the exception of reproductive disease, animals are usually asymptomatic. Goats sometimes have a poor appetite and are depressed for 1 to 2 days before an abortion. Clinical signs including fever, anorexia, mild coughing, rhinitis and increased respiratory rates occur in experimentally infected sheep but have not been reported in natural infections. Experimentally infected cats develop fever and lethargy.

Communicability

Yes. Large numbers of organisms are found in the placenta, fetal fluids, aborted fetus, milk, urine and feces. Serologically negative animals may shed organisms.

Diagnostic Tests

C. burnetii can be detected in vaginal discharges, the placenta, placental fluids and aborted fetuses, as well as milk, urine and feces. Organisms are not shed continuously in milk and colostrum. In the placenta, organisms can be identified in exudates or areas of inflammation with a modified Ziehl–Neelsen or Gimenez stain; *C. burnetii* is an acid–fast, pleomorphic, small coccoid or filamentous organism. This organism is not usually detected by Gram stains. Bacterial identity can be confirmed by immunohistochemistry. Polymerase chain reaction techniques are also available in some laboratories. Fresh, frozen or paraffin–embedded samples of serum, buffy coat, milk, feces, vaginal exudates, cerebrospinal fluid, bone marrow, placenta, liver, cardiac valve, fetal tissue and other tissues can be tested by PCR.

A number of serologic tests are available; the most commonly used tests include indirect immunofluores-

cence, enzyme–linked immunosorbent assay (ELISA) and complement fixation. Cross–reactions have been seen between some strains of *C. burnetii* and Chlamydia in ELISA and immunoblot assays.

C. burnetii can be isolated in cell cultures, embryonated chicken eggs or laboratory animals including mice, hamsters and guinea pigs; however, isolation is dangerous to laboratory personnel and is rarely used for diagnosis.

Treatment and Vaccination

Little is known about the efficacy of antibiotic treatment in ruminants or other domestic animals. Treatment is sometimes recommended to reduce the risk of abortion. Antibiotics may in some cases suppress rather than eliminate infections. Isolating infected pregnant animals and burning or burying the reproductive membranes and placenta can decrease transmission.

Vaccines are not available for domestic ruminants in the United States but are used in other countries. Vaccines may prevent infections in calves, decrease shedding of organisms and improve fertility in infected animals. They do not eliminate shedding of the organism.

Morbidity and Mortality

Information on the prevalence of infection is limited. In an endemic region in California, 18 to 55% of sheep had antibodies to *C. burnetii*; the number of seropositive sheep varied seasonally and was highest soon after lambing. In other surveys, 82% of cows in some California dairies were seropositive, as well as 78% of coyotes, 55% of foxes, 53% of brush rabbits and 22% of deer in Northern California. In Ontario, Canada, infections were found in 33 to 82% of cattle herds and 0 to 35% of sheep flocks. Close contact with sheep appears to increase the risk of infection in dogs.

Significant morbidity can be seen in some species. In sheep, abortions can affect 5 to 50% of the flock. In one California study, Q fever may have been responsible for 9% of all abortions in goats. Deaths are rare in natural infections.

Post–Mortem Lesions

Placentitis is the most characteristic sign in ruminants. The placenta is typically leathery and thickened and may contain large quantities of white–yellow, creamy exudate at the edges of the cotyledons and in the intercotyledonary areas. In some cases, the exudate may be reddish– brown and fluid. Severe vasculitis is uncommon, but thrombi and some degree of vascular inflammation may be noted. Fetal pneumonia has been seen in goats and cattle and may occur in sheep; however, the lesions in aborted fetuses are usually non–specific.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Material Safety Data Sheets –Canadian Laboratory Center for Disease Control http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology
http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines
http://www.oie.int/eng/normes/mmanual/a_summry.htm

Q Fever: An Overview
United States Animal Health Association
http://www.usaha.org/speeches/speech01/s01conch.html

The Merck Manual
http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook
http://www.vnh.org/BIOCASU/toc.html

References

"Control of Communicable Diseases." Edited by J. Chin. American Public Health Association, 2000, pp.407–411.

De la Concha–Bermejillo, A., E.M. Kasari, K.E. Russell, L.E. Cron, E.J. Browder, R. Callicott and R.W. Ermel1. "Q Fever: An Overview. *United States Animal Health Association*. 4 Dec 2002 <http://www.usaha.org/speeches/speech01/s01conch.html>.

Marrie, T.J. *Q Fever.* Edited by S.R. Palmer, E.J.L. Soulsby and D.I.H Simpson. New York: Oxford University Press, 1998, pp. 171–185.

Martin J. and P. Innes. "Q Fever." *Ontario Ministry of Agriculture and Food,* Sept 2002. 4 Dec 2002 <http://www.gov.on.ca/OMAFRA/english/livestock/vet/facts/info_qfever.htm>.

"Material Safety Data Sheet –*Coxiella burnetii*." *Canadian Laboratory Centre for Disease Control*, January 2001. 2 Dec 2002 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds43e.html>.

"Q Fever." In *Manual of Standards for Diagnostic Tests and Vaccines*. Paris: Office International des Epizooties, 2000, pp. 822–831.

"Q Fever." In *Medical Management of Biological*

Casualties Handbook, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 2 Dec 2002 <http://www.vnh.org/BIOCASU/10.html>.

"Q Fever." In *The Merck Manual*, 17th ed. Edited by M.H. Beers and R. Berkow. Whitehouse Station, NJ: Merck and Co., 1999. 7 Oct 2002 < http://www.merck.com/pubs/mmanual/section13/chapter159/159i.htm>.

"Q Fever." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 486–7.

Van der Lugt, J, B. van der Lugt and E. Lane. "An approach to the diagnosis of bovine abortion." Paper presented at the mini–congress of the Mpumalanga branch of the SAVA, 11 March 2000. Pathology for the practicing veterinarian, Large Animal Section, no. 1 (April 2000). 2 December 2002 <http://vetpath.vetspecialists.co.za/large1.htm>.

Walker, D.H. "Rickettsiae." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 3 December 2002 <http://www.gsbs.utmb.edu/microbook/ch038.htm>.

Tularemia

rabbit fever, deerfly fever, Ohara's disease, Francis disease

Last Updated: Jan. 2004

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Tularemia results from infection by *Francisella tularensis* (formerly known as *Pasteurella tularensis*), a Gram negative, non–motile coccobacillus. Two subspecies exist: *F. tularensis tularensis* (also known as Jellison type A) and *F. tularensis holarctica* (Jellison type B). *F. tularensis tularensis* is found in lagomorphs in North America and is highly virulent for humans and domestic rabbits; *F. tularensis* holarctica is less virulent and occurs in beaver, muskrats and voles in North America and in hares and small rodents in Eurasia.

Geographic Distribution

Tularemia occurs in North America, continental Europe, Russia, China and Japan. The subspecies *F. tularensis tularensis* is found in North America; *F. tularensis holarctica* is seen in North America and Eurasia.

Transmission

F. tularensis can be transmitted by ingestion, inhalation, arthropod–borne transfer or direct contact through the skin and mucous membranes. Organisms are found in the blood and tissues of infected animals and can survive for long periods on fomites including food and water. Aquatic animals may develop tularemia after being immersed in contaminated water. Carnivores sometimes become infected after ingesting a contaminated carcass. Vectors for *F. tularensis tularensis* include ticks (including *Dermacentor andersoni*, *D. variabilis* and *Amblyomma americanum*) and biting flies (particularly deerflies). *F. tularensis holarctica* is also transmitted by mosquitoes in Russia. Rarely, the organism is spread by animal bites.

F. tularensis can survive for long periods of time in arthropod vectors and in the environment. Individual flies may carry the organism for 2 weeks and ticks throughout their lifetimes. Viable bacteria can also be found for weeks to months in the carcasses and hides of infected animals and in fomites including grain dust, straw, water, soil and bedbugs. This organism is highly resistant to freezing; live organisms have been found after 3 years in rabbit meat stored at –15° C. *F. tularensis* has been weaponized.

Disinfection

F. tularensis is easily killed by disinfectants including 1% hypochlorite, 70% ethanol, glutaraldehyde and formaldehyde. It can also be inactivated by moist heat (121° C for at least 15 min) and dry heat (160–170° C for at least 1 hour). This bacterium remains viable at freezing temperatures for months to years.

Infections in Humans

Incubation Period

The incubation period in humans is 3 to 15 days; clinical signs usually appear after 3 to 5 days.

Clinical Signs

Six forms of tularemia are seen in humans: typhoidal, ulceroglandular, glandular, oculoglandular, oropharyngeal and pneumonic. The form of the disease depends on the inoculation site.

Typhoidal tularemia usually occurs after inhalation but can also develop after skin inoculation or ingestion. The clinical signs may include fever, prostration, headache, nausea and weight loss. Some patients become extremely weak and develop recurring chills and drenching sweats. A nonspecific rash may be seen but lymphadenopathy is usually absent. Pneumonia is particularly common in the typhoidal form and can be severe.

Ulceroglandular tularemia usually occurs after infection through the skin or mucous membranes. The clinical signs may include fever, chills, headache and malaise. The regional lymph nodes are typically enlarged and painful; they may suppurate and drain profusely. An inflamed papule usually develops where the initial

transmission occurred; it quickly turns into a pustule then ulcerates. On the extremities, single ulcers with thin, colorless, scanty exudates are usual. Glandular tularemia is characterized by fever and tender lymphadenopathy without a skin ulcer. Infection of the conjunctiva results in oculoglandular tularemia; this form is characterized by painful, unilateral, purulent conjunctivitis with preauricular or cervical lymphadenopathy. In some cases, there may be chemosis, periorbital edema and multiple small nodules or ulcerations on the conjunctiva. When the ulceroglandular disease occurs only in the throat, it is called oropharyngeal tularemia. In this form, there is an acute exudative or membranous pharyngotonsillitis with cervical lymphadenopathy.

Pneumonic tularemia can occur after inhalation or by secondary hematogenous spread. Victims develop severe, sometimes fulminant, atypical pneumonia. There may be signs of lung consolidation and, in come cases, delirium. Sometimes, the only symptoms may be a dry, unproductive cough, with decreased breath sounds and substernal discomfort. The pneumonic form can occur with any other form and has a high mortality rate. It develops in 10 to 15% of all cases of ulceroglandular tularemia and about 50% of cases of typhoidal tularemia.

Communicability

Person to person transmission has not been seen; however, infectious organisms can be found in the blood and other tissues.

Diagnostic Tests

Tularemia is often diagnosed by immunofluorescent staining of *F. tularensis* antigens in tissue samples or blood, and by serology. Commonly used serologic tests include tube agglutination, microagglutination and enzyme–linked immunosorbent assays (ELISA). A rising titer is diagnostic. Significant titers begin to appear during the second week of infection, although some specific antibodies are seen within the first 7 days. Cross–reactions occur with Brucella species, Proteus OX19, and Yersinia.

Tularemia can also be diagnosed by isolating *F. tularensis* from blood, sputum, pharyngeal or conjunctival exudates, ulcers, lymph nodes and gastric washings. *F. tularensis* does not grow well on standard media but may be isolated on media containing cysteine or sulfhydryl compounds. On McCoy medium, colonies are small, prominent, round and transparent. Confluent, milky, mucoid colonies develop on Francis medium and modified Thayer/Martin agar. Growth is slow and may take up to 3 weeks. Identification is by the absence of growth on ordinary media, morphology, immunofluorescence and slide agglutination. Organisms are non–motile, Gram negative small coccobacilli, with bipolar staining in young cultures. Bacteria from older cultures may be pleomorphic. *F. tularensis tularensis* can be distinguished from *F. tularensis* palaearctica by glycerol fermentation, ri*bos*omal RNA probes and polymerase chain reaction (PCR) tests. Organisms in culture are highly infectious to humans and special precautions must be taken during isolation.

Treatment and Vaccination

F. tularensis is susceptible to a variety of antibiotics. Relapses are not common but can occur if treatment is stopped before all bacteria are eliminated. Live attenuated vaccines may be recommended for people at a high risk of infection, such as laboratory workers.

Morbidity and Mortality

Tularemia can affect all ages. Infections occur most often in hunters, butchers, farmers, fur handlers and laboratory workers. In natural infections, ulceroglandular tularemia is the most common form; it occurs in 75 to 85% of cases. The typhoidal form is seen in 5 to 15%, the glandular form in 5–10% and the oculoglandular form in 1 to 2%. Typhoidal tularemia would be expected to be the predominant form after an attack by aerosolized *F. tularensis* in a biological weapon.

The mortality rate is approximately 30 to 35% for untreated *F. tularensis tularensis* infections and 5 to 15% for *F. tularensis holarctica* infections. Typhoidal tularemia is the most dangerous form; if untreated, the case fatality rate is approximately 35%. In contrast, the case fatality rate for the untreated ulceroglandular form is 5%. Naturally acquired cases are rarely fatal if treated; case fatality rates up to 1–3% are cited by some authorities. Higher fatality rates would be expected after a biological attack. Permanent immunity usually develops after a single episode of tularemia.

Infections in Animals

Species Affected

More than a hundred species of animals can be infected with F. tularensis. The natural hosts include cottontail and jack rabbits, hares, voles, vole rats, squirrels, muskrat, beaver and lemmings. Among domestic animals, sheep seem to be particularly susceptible to clinical disease. Tularemia has also been seen in dogs, cats, pigs and horses; cattle seem to be resistant. Infections in birds, reptiles and fish have been reported.

Incubation Period

The incubation period is 1 to 10 days.

Clinical Signs

The full spectrum of clinical signs is not known in animals. Many cases may be asymptomatic. Signs of septicemia can be seen in sheep and other mammals; symptoms may include fever, lethargy, anorexia, stiffness, increased pulse and respiration, coughing, diarrhea and pollakiuria. Rabbits and rodents may be depressed,

anorectic and ataxic, with a roughened coat and tendency to huddle. Anorexia, weight loss and vomiting have been reported in cats. Skin lesions are rarely seen in animals. Symptoms usually last 2 to 10 days in susceptible animals and may end in prostration and death. Susceptible species may be found dead without other symptoms.

Communicability

Yes. Infectious organisms can be found in the blood, tissues and feces. Humans and other animals can be infected through the skin or mucous membranes; routes of transmission include aerosols and ingestion. Infected cats may be able to transmit the organism in bites.

Diagnostic Tests

Impression smears of liver, spleen, bone marrow, kidney, lung or blood may be helpful for a presumptive diagnosis; small Gram negative coccobacilli can sometimes be found inside cells and scattered among tissue debris. *F. tularensis* is very small (0.2–0.7 µm) and easy to miss. Definitive diagnosis is by immunofluorescent detection of organisms in impression smears from these tissues, agglutination with specific antiserum, culture and occasionally serology. Animal inoculation can be used but it is dangerous and not recommended for routine identification.

F. tularensis can be isolated from enlarged lymph nodes, blood and tissues including liver, spleen and bone marrow; overgrowth of other bacteria may prevent recovery from animals found dead. This organism does not grow well on standard media but can be isolated on media containing cysteine or sulfhydryl compounds. On McCoy medium, colonies are small, prominent, round and transparent. Confluent, milky, mucoid colonies develop on Francis medium and modified Thayer/Martin agar. Growth is slow and may take up to 3 weeks. Identification is by the absence of growth on ordinary media, morphology, immunofluorescence and slide agglutination. The organisms are non–motile, Gram negative, small coccobacilli, with bipolar staining in young cultures. Bacteria from older cultures may be pleomorphic. *F. tularensis tularensis* can be distinguished from *F. tularensis holarctica* by glycerol fermentation, ri*bos*omal RNA probes and polymerase chain reaction (PCR) tests. Organisms in culture are highly infectious to humans and special precautions must be taken during isolation.

Serology is occasionally useful. Species sensitive to tularemia typically die before specific antibodies develop; however, significant titers can be found in more resistant species such as sheep, cattle, pigs, moose, dogs and birds. Available tests include tube agglutination and enzyme–linked immunosorbent assay (ELISA).

Treatment and Vaccination

Tularemia can be treated with various antibiotics but long–term treatment may be necessary; early treatment is expected to reduce mortality. Vaccines are not marketed specifically for animals.

Morbidity and Mortality

Tularemia is relatively common and often fatal in wild animals; disease is particularly common among rabbits, rodents, pheasants and quail. This disease is rare among domestic rabbits and rodents, but may be seen in animals kept outside. Outbreaks of *F. tularensis tularensis* infections, characterized by high mortality, have been seen in sheep. Mortality rates up to 15% are seen in untreated lambs.

Post–Mortem Lesions

Most animals with acute tularemia are in good body condition. The most consistent lesions are miliary, grayish–white necrotic foci in the liver and sometimes the spleen, bone marrow and lymph nodes. Some of these necrotic foci may be barely visible. Enlargement of the liver, spleen and lymph nodes is also common. In rabbits, the white necrotic foci on a dark, congested liver and spleen have been compared to the Milky Way. Congestion and edema is frequent in the lungs; consolidation and fibrinous pneumonia or pleuritis may also be found. The abdominal cavity sometimes contains fibrin. In some species, the lesions can resemble tuberculosis and chronic granulomas may be found in the liver, spleen, kidneys and lungs.

Internet Resources

Centers for Disease Control and Prevention (CDC) Tularemia Pages

http://www.bt.cdc.gov/agent/tularemia/index.asp

Material Safety Data Sheets–Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

References

"Bacterial infections caused by Gram–negative bacilli. Enterobacteriaceae." In *The Merck Manual*,

17th ed. Edited by M.H. Beers and R. Berkow. Whitehouse Station, NJ: Merck and Co., 1999. 8 Nov 2002 <http://www.merck.com/pubs/mmanual/section13/chapter157/157d.htm>.

Biberstein, E.L. and J. Holzworth. "Bacterial Diseases. Tularemia." In *Diseases of the Cat*. Edited by J. Holzworth. Philadelphia, PA: W.B. Saunders, 1987, p. 296.

Collins, F.M. "Pasteurella, Yersinia, and Francisella." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 20 November 2002 < http://www.gsbs.utmb.edu/microbook/ch029.htm>.

"Control of Communicable Diseases." Edited by J. Chin. American Public Health Association, 2000, pp.532–535.

"Material Safety Data Sheet –*Francisella tularensi*s." *Canadian Laboratory Centre for Disease Control*, May 2001. 20 November 2002 <http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/msds68e.html>.

Pearson, A. In *Zoonoses*. Edited by S.R. Palmer, E.J.L. Soulsby and D.I.H Simpson. New York: Oxford University Press, 1998, pp. 267–279.

"Tularemia." In *Manual of Standards for Diagnostic Tests and Vaccines*. Paris: Office International des Epizooties, 2000, pp. 756–761.

"Tularemia." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 19 Nov 2002 <http://www.vnh.org/BIOCASU/11.html>.

"Tularemia." In *The Biology and Medicine of Rabbits and Rodents*, 2nd ed. Edited by J.E. Harkness and J.E. Wagner. Philadelphia: Lea and Febiger, 1977, pp. 179–80.

"Tularemia." In *The Merck Veterinary Manual*, 8th ed. Edited by S.E. Aiello and A. Mays. Whitehouse Station, NJ: Merck and Co., 1998, pp. 494–5; 1394.

Viral Hemorrhagic Fevers–Ebola and Marburg

African Hemorrhagic Fever

Last Updated: Apr. 2005

Institute for International Cooperation in Animal Biologics
An OIE Collaborating Center
Iowa State University
College of Veterinary Medicine

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY

Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: (515) 294–7189
FAX: (515) 294–8259
E–mail: cfsph@iastate.edu
Web: http://www.cfsph.iastate.edu

Etiology

Ebola and Marburg are caused by Ebola virus and Marburg virus, the only members of the family Filoviridae. These two viruses are closely related and are considered to be serotypes or genotypes within a single genus. Ebola virus is subdivided into four subtypes: Zaire, Sudan, Reston, and Côte d'Ivoire.

Geographic Distribution

Ebola-Zaire, Ebola-Sudan, and Ebola-Côte d'Ivoire outbreaks have been seen in Sudan, Zaire, the Ivory Coast and the Democratic Republic of the Congo. Ebola-Reston outbreaks have occurred in non-human primates in the Italy and United States; these outbreaks were traced to monkeys imported from the Philippines. Wild non-human primates in the Philippines may have antibodies to Ebola-Reston.

Marburg has been seen in Angola, Uganda, Kenya, Zimbabwe and South Africa. Outbreaks also occurred in Germany and former Yugoslavia, in humans exposed to African green monkeys from East Africa.

Transmission

Human filovirus outbreaks seem to have a zoonotic source, but the reservoir host has not been identified although bats have been implicated in Marburg. Transmission among humans and other primates is by direct contact with infected blood, secretions, organs or semen, and on fomites. Virus has also been found in urine. Marburg and Ebola can be transmitted by aerosols and small droplets among monkeys; however, aerosol transmission does not appear to be a major route of spread between humans infected with Ebola. Filoviruses can survive for several weeks in blood and corpses.

Disinfection

Hypochlorite or phenolic disinfectants are generally recommended for disinfection. Ebola virus is susceptible to 2% sodium hypochlorite, 2% glutaraldehyde, 5% peracetic acid and 1% formalin. This virus is also inactivated by ultraviolet light, gamma irradiation, 0.3% betapropiolactone for 30 minutes at 37° C, or heating to 60° C for 1hr. Marburg virus is susceptible to 1% sodium hypochlorite, 2% glutaraldehyde or formaldehyde, ultraviolet light or heat.

Infections in Humans

Incubation Period

The incubation period is 2 to 21 days for Ebola and 3 to 10 days for Marburg.

Clinical Signs

Ebola usually begins with the abrupt onset of headache, sore throat, fever, myalgia, joint pain and weakness, followed by diarrhea, vomiting and stomach pain. A maculopapular rash on the truck, red eyes and hiccups are also seen. Hemorrhages are common and may include petechiae, ecchymoses, bloody diarrhea, bleeding from puncture sites and mucous membranes, and other internal and external bleeding. Early symptoms may be nonspecific and resemble other illnesses. Ebola-Reston can infect humans but hemorrhagic illnesses have not been seen.

The symptoms of Marburg are very similar to Ebola. This disease also begins with the acute onset of fever, chills, headache and myalgia. Approximately five days later, a maculopapular rash may appear on the trunk, followed by a sore throat, nausea, vomiting, chest pain, abdominal pain or diarrhea. Other symptoms may include severe weight loss, jaundice, delirium, shock, pancreatitis, liver failure, massive hemorrhaging and multi-organ dysfunction.

Communicability

Filoviruses can be spread between humans by contact with blood, secretions, organs, or semen. Ebola virus has been found in large quantities in the skin. Aerosol transmission is at least theoretically possible.

Viral Hemorrhagic Fevers–Ebola and Marburg

Diagnostic Tests

Early in the course of infection, Ebola can be diagnosed by an antigen-capture enzyme-linked immunosorbent assay (ELISA), virus isolation, detection of viral RNA by polymerase chain reaction (PCR) or the detection of virus-specific IgM by ELISA. Serology for IgG antibodies is useful later in the disease. At necropsy, immunohistochemistry, virus isolation or PCR can be employed.

Early Marburg infections can de diagnosed by antigen-capture ELISA, virus isolation, polymerase chain reaction (PCR) or an ELISA to detect Ebola-specific IgM. An IgG specific ELISA is useful later in the disease or after recovery. Diagnosis at necropsy is by immunohistochemistry on blood or tissue, virus isolation or PCR.

Treatment and Vaccination

No specific treatment is available for Ebola or Marburg; supportive therapy is given, with appropriate barrier precautions against infection of medical personnel. Transfusions of fresh-frozen plasma and other replacements for clotting proteins have been tried. Heparin has also been used, although its use is controversial.

Morbidity and Mortality

The case fatality rate is 50 to 90% for Ebola and 23 to 90% for Marburg. Bleeding is a poor prognostic sign. Ebola-Reston can infect humans but hemorrhagic illnesses have not been seen.

Infections in Animals

Species Affected

Ebola-Zaire, Ebola-Sudan and Ebola-Côte d'Ivoire affect humans and non-human primates; Ebola-Reston causes hemorrhagic fever in monkeys but does not seem to be pathogenic for humans. Naturally-occurring Ebola antibodies have been found in rhesus monkeys, African green monkeys, cynomolgus monkeys and baboons. Chimpanzees, gorillas, rhesus monkeys, vervet monkeys, cynomolgus monkeys, newborn mice and guinea pigs can develop clinical illness. Experimentally infected rabbits, pigeons and various species of mice, bats, frogs, geckos, snakes, tortoises and arthropods did not develop clinical signs; however, virus replication was seen in bats and possibly snakes, mice and spiders. The natural reservoir of this virus is unknown.

Marburg virus can infect humans and non-human primates, including African green monkeys. Antibodies have been found in captive vervet monkeys and baboons in Kenya. The natural host is unknown but bats have been implicated.

Incubation Period

The incubation period for Marburg or Ebola-Zaire infections in rhesus monkeys and African green monkeys is 4 to 16 days. In guinea pigs, the incubation period is 4 to 10 days.

Clinical Signs

Filovirus infections result in severe, often fatal, hemorrhagic fevers in non-human primates. Clinical signs may include fever, anorexia, vomiting, splenomegaly, weight loss and a skin rash. Hemorrhages can occur in any organ and may include petechiae, bleeding into the gastrointestinal tract, or bleeding from puncture wounds and mucous membranes. Guinea pigs infected with unpassaged virus from primates usually develop a fever and weight loss but recover; animals infected with serially passaged virus may develop fatal liver disease.

Communicability

Blood, secretions, organs, semen and urine may contain infectious virus; virus can probably be found almost anywhere in the body. Aerosol transmission of both Ebola and Marburg viruses has been seen in primates.

Diagnostic Tests

Filovirus infections can be diagnosed by virus isolation; Vero cells or MA-104 cells are commonly used for Ebola virus. In humans, Ebola virus is most reliably isolated from acute-phase serum but can also be found in throat washes, urine, semen, anterior eye fluid and other fluids. In necropsied monkeys, filoviruses have been found in particularly high concentrations in the liver, spleen, lungs and lymph nodes. Electron microscopy can also detect virus particles in tissues: filoviruses are pleomorphic, long and filamentous and may be branched. Some may be U-shaped, b-shaped or circular. Viral antigens can be detected with an enzyme-linked immunosorbent assay (ELISA) or by immunofluorescence. Skin biopsies collected into formalin may be helpful for diagnosis; large amounts of Ebola antigen have been found in skin. A reverse transcriptase-polymerase chain reaction (RT-PCR) assay can identify Marburg or Ebola RNA.

Serologic tests include indirect immunofluorescence assays (IFA), immunoblotting and ELISAs. Neutralization tests are unreliable for filoviruses. Paired serum samples should be tested; low IFA titers in single samples cannot be interpreted. The significance of antibody titers in asymptomatic primates is controversial.

Treatment and Vaccination

No specific therapy or vaccine is available.

Morbidity and Mortality

Marburg and Ebola infections have a very high mortality rate in non-human primates and experimentally infected suckling mice. Guinea pigs infected with Ebola

virus from primates usually recover; animals infected with serially passaged virus may develop fatal liver disease.

Post-Mortem Lesions

At necropsy, there may be widespread petechiae and hemorrhages. Hemorrhages can occur in any organ but are particularly common in the gastrointestinal tract, kidneys, and pleural, pericardial and peritoneal spaces. The liver and spleen may be swollen and friable. Animals may have a maculopapular rash. There can also be signs of interstitial pneumonia, nephritis, and necrosis of the liver, lymphoid tissue, adrenal cortex or pulmonary epithelium.

Internet Resources

Centers for Disease Control and Prevention (CDC) –Viral Hemorrhagic Fevers Index

http://www.bt.cdc.gov/agent/vhf/index.asptm

"Marburg and Ebola Viruses" in Encyclopedia of Virology

http://www.bocklabs.wisc.edu/eov-ebola.html

Material Safety Data Sheets– Canadian Laboratory Center for Disease Control http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

Pathology of Nonhuman Primates from Primate Info Net. Wisconsin Primate Research Center

http://www.primate.wisc.edu/pin/pola6-99.html

Primate Info Net. Wisconsin Primate Research Center

http://www.primate.wisc.edu/pin/

Proceedings of an international colloquium on Ebola virus infection and other hemorrhagic fevers held in Antwerp, Belgium, 6-8 December, 1977 http://www.itg.be/ebola/

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

References

Baskin, G.B. "Pathology of Nonhuman Primates." Primate Info Net. Wisconsin Primate Research Center, Feb, 2002. 23 Oct 2002 <http://www.primate.wisc.edu/pin/pola6-99.html>.

Bowen E.T., G.S. Platt, D.I. Simpson, L.B. McArdell and R.T. Raymond. "Ebola haemorrhagic fever: experimental infection of monkeys." Trans. R. Soc. Trop. Med. Hyg. 72, no. 2 (1978): 188-91.

Chepurnov, A.A., A.A. Dadaeva and S.I. Kolesnikov. "Study of the pathogenesis of Ebola fever in laboratory animals with different sensitivity to the virus." Bulletin of Experimental Biology and Medicine 132, no. 6 (December 2001): 1182-6.

Dalgard, D.W.R.J. Hardy, S.L. Pearson, G.J. Pucak, R.V. Quander, P.M. Zack, C.J. Peters and P.B. Jahrling. "Combined simian hemorrhagic fever and Ebola virus infection in cynomolgus monkeys." American Association for Laboratory Animal Science 42, no. 2 (Apr 1992): 152-157.

Drosten C., S. Gottig, S. Schilling, M. Asper, M. Panning, H. Schmitz and S. Gunther. "Rapid detection and quantification of RNA of Ebola and Marburg viruses, Lassa virus, Crimean-Congo hemorrhagic fever virus, Rift Valley fever virus, dengue virus, and yellow fever virus by real-time reverse transcription-PCR." J. Clin. Microbiol. 40, no. 7 (July 2002): 2323-30.

"Ebola Hemorrhagic Fever." *Centers for Disease Control and Prevention (CDC)*, June 2002. 8 Nov 2002 <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebola.htm>.

Feldmann H and H-D Klenk. "Filoviruses." In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 11 Oct 2002 <http://www.gsbs.utmb.edu/microbook/ch072.htm>

Johnson B.K., L.G. Gitau, A. Gichogo, P.M. Tukei, J.G. Else, M.A. Suleman, R. Kimani and P.D. Sayer. "Marburg, Ebola and Rift Valley Fever virus antibodies in East African primates." Trans. R. Soc. Trop. Med. Hyg. 76, no. 3 (1982): 307-10.

Klenk, H-D, W. Slenczka and H Feldmann. "Marburg and Ebola Viruses." In Encyclopedia of Virology. Edited by Robert G. Webster and Allan Granoff. Academic Press Ltd, 1995. 15 Oct 2002 <http://www.bocklabs.wisc.edu/eov-ebola.html>.

Ksiazek TG, C.P. West, P.E. Rollin, J.B. Jahrling and C.J. Peters. "ELISA for the detection of antibodies to Ebola viruses." J. Infect. Dis. 179 Suppl 1 (Feb 1999): S192-8.

"Marburg Hemorrhagic Fever." *Centers for Disease Control and Prevention (CDC)*, April 2002. 8 Nov 2002 <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/marburg.htm>.

"Material Safety Data Sheet –Ebola virus" *Canadian Laboratory Centre for Disease Control*, April 2001. 11 October 2002 <http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/msds53e.html>.

"Material Safety Data Sheet –Marburg virus" *Canadian Laboratory Centre for Disease Control*, 1996. 11 October 2002 <http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/msds98e.html>.

Murphy, F.A. "Pathology of Ebola Virus Infection." In Proceedings of an international colloquium on

Ebola virus infection and other hemorrhagic fevers held in Antwerp, Belgium, 6-8 December, 1977. 28 Oct 2002 <http://www.itg.be/ebola/ebola-17.htm>.

Peters, C.J. and J.W. LeDue. "An introduction to Ebola: the virus and the disease." J. Infect. Dis. 179, Suppl 1 (1999):ix-xvi.

Swanepoel R, P.A. Leman, F.J. Burt, N.A. Zachariades, L.E. Braack LE, T.G. Ksiazek, P.E. Rollin, S.R. Zaki and C.J. Peters. "Experimental inoculation of plants and animals with Ebola virus." *Emerg. Infect. Dis.* 2, no. 4 (Oct-Dec 1996): 321-5.

"Viral Hemorrhagic Fevers." In *Medical Management of Biological Casualties Handbook*, 4th ed. Edited by M. Kortepeter, G. Christopher, T. Cieslak, R. Culpepper, R. Darling J. Pavlin, J. Rowe, K. McKee, Jr., E. Eitzen, Jr. Department of Defense, 2001. 24 Oct 2002 < http://www.vnh.org/BIOCASU/15.html >.